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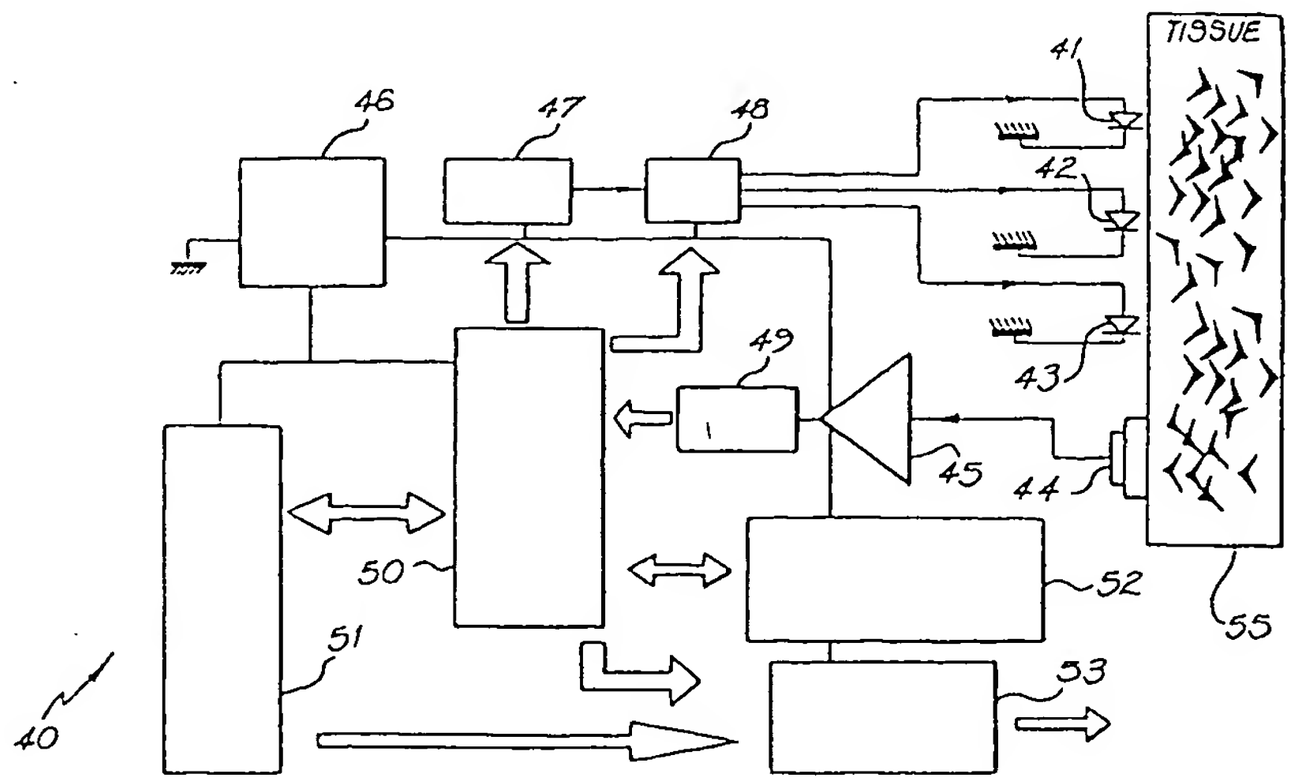

(57) Abstract

A non-invasive method for determining the absolute level of oxygen saturation in blood in deep tissue including the steps of irradiating a target area of tissue with radiation of at least two distinct wavelengths at rest and after voluntarily hydrostatically perturbating the venous blood volume in the target tissue, providing a first set of signals that represents the absorption of the radiation at each wavelength at rest and a second set of signals that represents the absorption of the radiation at each wavelength after perturbation of the blood, subtracting the first set of signals from the second set of signals to provide a difference signal for each wavelength that represents the venous blood volume change as a consequence of the perturbation, and determining the ratio of the difference signals and comparing that ratio with the ratio determined in vitro to provide the absolute level of blood oxygen concentration. The method is carried out using a spectrometer (40) having three transmitting optodes (41, 42, 43) and a receiving optode (44).

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NON-INVASIVE DETERMINATION OF OXYGEN SATURATION IN BLOOD IN DEEP TISSUE

TECHNICAL FIELD

This invention relates to the non-invasive measurement of oxygen saturation in blood.

BACKGROUND ART

Recent developments in dual wavelength near infrared spectroscopy (near infrared spectrometer) suggests that this measurement technique, which measures the oxyhemoglobin-to-deoxyhemoglobin ratio, would provide many of the attributes required for continuous non-invasive assessment of cerebral blood-oxygen saturation. US Patent No 4,223,680 discloses a method in which near infrared radiation is reflected by the brain or other tissue to measure an absorption ratio at two wavelengths that characterises the proportion of cerebral blood-oxygen levels. The specification notes the advantages of using the isobestic wavelength in the dual wave system which eliminates the effects of changes in blood volume when measuring cerebral blood-oxygen changes. For hemoglobin, the isobestic wavelength is between 805 and 815 nm in the infrared. At this wavelength, there is a change in a spectrometric absorption due to hemoglobin concentration but not to changes in hemoglobin oxygen content.

The US specification further described the use of contrabestic wavelengths to achieve the same ends. The contrabestic wavelengths represents two specific wavelengths that straddle the isobestic wavelength such that their net difference represents changes due to oxygen binding by hemoglobin. Typically, contabestic wavelengths of hemoglobin are ~790

nm and 850 nm. The difference signal, 790-850 nm provides the blood oxygen desaturation level.

A number of biomolecules absorb near infrared radiation (between 700nm to 1,300nm) at specific wavelengths via bond stretching and/or dipole interactions. Hemoglobin, has a strong absorption peak at ~800 nm. This absorption is independent of its oxygen binding state, hence it is referred to as hemoglobins' isobestic wavelength. Whereas, at a wavelength of 760 nm, deoxyhemoglobin (deoxygenated blood) has a significantly higher absorption when compared to oxyhemoglobin (oxygenated blood).

A comparison between the hemoglobin absorption at 760 nm to that at 805 nm gives an index for relative oxy- and deoxyhemoglobin concentrations. Further, at these wavelengths, the radiation has good biological tissue penetration and while subject to extensive scattering, has a low tissue absorption coefficient compared to that of hemoglobin.

The absorption coefficient is defined by Beer-Lambert relationship as:

$$\mu_a = 1/L \ln I/I_o = \varepsilon [C]$$

where μ_a = absorption coefficient,

L = part length,

I_o = initial radiation,

λ = reflected (transmitted radiation), and

ε = extinction coefficient

[C] = the concentration of the absorbing media, in this case hemoglobin. Ignoring the much lower absorption levels of tissue then, hemoglobin oxygen saturation, Y is given by

$$Y = H_bO_2 / H_b + H_bO_2 \qquad (1)$$

where:-

(H_bO_2 = oxyhemoglobin and

H_b = deoxyhemoglobin)

For each wavelength (eg. $\lambda_1 = 760nm$ and $\lambda_2 = 805nm$),

$$\mu_a = \varepsilon Hb[Hb] + \varepsilon HbO_2[HbO_2] \quad (2)$$

The components within the brackets [ ] indicates concentration.

When taken as a ratio, λ_1/λ_2 and considering that at λ_2 the absorption response of hemoglobin is insensitive to its oxygenation state (eg. its isobestic wavelength) then:

$$\lambda_1/\lambda_2 = \mu_{a1}/\mu_{a2} = \varepsilon Hb_1/\varepsilon Hb_2 + \varepsilon Hb_1O_2 - Hb_1/\varepsilon Hb_2 .Y \quad (3)$$

As there is only a 40 nm difference between λ_1 and λ_2, their scattering coefficients (μ_s) in tissue are essentially the same. From equation 3, it is seen that the relative oxyhemoglobin levels are independent of concentration and hence, blood volume.

The extinction coefficient (ε) for hemoglobin is known (0.25 cm^{-1} mM^{-1} at 760 nm and <0.01 cm^{-1} mM^{-1} at 800 nm, obtained from *in vitro* Near infrared spectroscopy studies, Chance et al., 1988 along with the absorption coefficient at each wavelength (μ_{a1} and μ_{a2}) and thus the attenuation of those wavelengths with hemoglobin can be calculated.

The accuracy of equations 2 and 3 is limited by ignoring the extent of tissue (non-hemoglobin) absorption and the heterogeneity of the scattering properties of the tissue. Otherwise the measurement of the ratio of these two wavelengths give the proportion of blood oxygen saturation in tissue being irradiated.

The new infrared spectroscopy based methods and apparatus of the invention may be used to monitor physiological conditions such as sleep

apnea, patient exercise in heart failure, sudden infant death syndrome and muscle condition.

Sleep apnea is a condition in which a sufferer discontinues breathing for short periods of time during sleep. By far the most common cause of sleep apnea is the closure of the upper air passage. This is associated with loss of muscle tone of the soft palate. The consequences of this condition results in a reduced air passage in the nasopharynx region. In severe apnea, blockages occur over one hundred times a night with breathing pauses of up to two minutes. This results in hypoxia, reduced blood oxygen saturation, at which point the sufferer is aroused and breathing resumes. The most obvious symptom of sleep apnea is chronic tiredness, snoring and continual arousal from sleep.

Some 4% of the population is thought to be afflicted by apnea, and there is evidence that up to 10% of the male population over 40 years old may be sufferers. It is suggested that sleep apnea is the most under diagnosed medical condition today. In severe cases of sleep apnea, the reduced blood oxygen levels lead to cardiac arrhythmia, brain damage as well as a degraded quality of life. There is also evidence that day time hyper-somnolence induced by sleep apnea is a major cause of home, work and vehicular accidents. Consequently, it has been referred to as a major health hazard requiring more resources and attention.

Diagnosis of sleep apnea usually involves an overnight stay in a sleep clinic where the patient is monitored by instruments during sleep. This includes overnight monitoring of the heart signal (ECG), heart rate, brain wave signal (EEG), blood oxygen monitoring (pulse oximetry), eye and body movement strain gauges and respiratory gas flow monitoring. These instruments provide information on the effects of hypoxia (low blood

oxygen saturation), time and number of non-breathing events, the number of arousal's, quality of sleep, cerebral and cardiac effects. Hence the sleep clinic's costs are high, which makes sleep apnea diagnosis expensive.

Prior art pulse oximetry measures blood oxygen saturation non-invasively. In sleep apnea, as with many other medical conditions, oximetry provides a measure of blood oxygen desaturation. As reduced blood oxygen levels are a major sign of sleep apnea, pulse oximetry is one of the major monitoring instruments used in sleep clinics. Oximetry uses calibrated optical information to determine blood oxygen levels. In its most common construction, light emitting diodes (LED's) at 660 nm and 940 nm are used to irradiate the skin. These LED's are pulsed alternately with the photons reflected from the skin tissue being detected by a photodiode. The reflected 660 nm photons from the skin differentiate between the oxygenated blood (**oxyhemoglobin**) in blood vessels compared to the deoxygenated blood (**deoxyhemoglobin**).

Thus, by using an algorithm the percentage of blood oxygen saturation can be determined from the absorption level of the 660 nm photons compared to the base line derived from the 940 nm photons.

Pulse oximetry is a refinement of oximetry which utilises the pulsatile effect of blood flow in the arteries (pressure plus flow changes with the heart beat). In this implementation of oximetry, the reflected 940 nm photons from the skin are used to measure the pulse wave peak. It is at this point that newly oxygenated blood perfuses through the capillary bed. This optimises the blood oxygen saturation measurements in the arterial vessels thus optimising arterial blood oxygen saturation measurements.

At high blood oxygen saturation levels, pulse oximetry is reputedly a reliable measure of the percentage of arterial blood oxygen saturation.

Although this method does not pick up oxidised hemoglobin, on average, 1% of blood hemoglobin is in the oxidised form (not to be confused with the oxygenated form, oxyhemoglobin). As well, endogenously produced carbon monoxide combines with another 1% of the blood hemoglobin but is measured as oxyhemoglobin in oximetry. This 2% error is generally allowed for by adjustments in the algorithm used in oximetry measurements. However, in smokers, the carbon monoxide-hemoglobin concentration can be as high as 15%, and is commonly at a 5% level. This significantly reduces the accuracy of oximetry which "sees" the carbon monoxide bound hemoglobin as oxyhemoglobin.

The accuracy of pulse oximetry (ignoring the carbon monoxide-hemoglobin concentration) is only reliable down to approximately 80% blood oxygen saturation, at which point the linear relationship with 660 nm photon absorption is no longer true At below 50% blood oxygen saturation pulse Oximeters have no specified accuracy which makes Pulse oximetry unsuitable for the determination of blood oxygen saturation for the profound hypoxia that may occur with sleep apnea.

Another disadvantage of pulse oximetry for sleep apnea monitoring is that it measures arterial blood oxygen levels rather than the venous levels. For example, with an hypoxic episode, the tissue builds up an oxygen debt. Hence once breathing is restored, the arterial blood oxygen levels rapidly return to normal (~95% saturation) but the increased tissue demand, brought about by the hypoxic event, results in a significantly higher oxygen extraction from the capillary bed for several minutes post event (arterial saturation is determined by lung and cardiac function whereas the venous saturation depends on the oxygen extraction by the tissue via the capillary bed). This is reflected in the depressed oxygen saturation of the venous

blood draining the tissue. Thus, although the arterial saturation readings suggest normal saturation levels, measurement of the venous blood oxygen levels will show otherwise.

The most critical failure of pulse oximetry is not only due to its limited accuracy at low blood oxygen saturation, nor the disadvantages of restricting the saturation measurement to the arterial rather than the venous blood. Its main flaw is due to the limited tissue penetration of photons at 660 nm, approximately ten millimetres. At this wavelength, returning photons penetrating more than several millimetres are generally attenuated, due to their high absorption by hemoglobin and tissue at this wavelength.

Non invasive use of oximetry is confined to the skin vascular measurements. The assembly of oximeters are designed as clamps for finger or earlobe attachment. Blood oxygen saturation readings are made from reflected photons from within the skin vascular bed.

Blood flow to the skin is highly variable. The skin vascular bed contains special vessels known as anastomoses (arterial-venous shunts) which allow the blood to by-pass the skin capillary bed, where oxygen exchange takes place. The main function of these shunts is thermo-regulation (body temperature control). But as the skin is the largest organ in the body, it also provides a blood reservoir function such that, when the main organs of the body (especially the brain and heart) are oxygen stressed, the heart rate is increased to provide greater blood flow to these organs and the less critical tissue, such as the skin is by-passed.

As well as the shunting by-pass, the arteriole vessels contract further reducing skin blood volume and flow. Hence during an hypoxic episode, the blood flow to the skin is minimal.

The change in blood oxygen concentration in the skin vascular bed is therefore decoupled from that in the major organs. Hence reading from pulse oximeters provide only a qualitative and not a reliable quantitative measure of deep tissue blood oxygen saturation in subjects with sleep apnea.

These limitations in monitoring blood oxygen saturation in sleep apnea results in oximetry being of limited diagnostic value. Despite low blood oxygen being the major sign in apnea, oximetry measurements can not provide reliable quantitative readings.

It is, therefore, an object of the invention to provide a means of assessing the changes in tissue blood oxygen levels, blood volume changes and heart rate for monitoring and diagnosis. Changes in blood oxygen levels reflect mainly that of the venous blood and this will provide relevant information on the oxygen stress that the brain is subject to and can be initially correlated to EEG readings as a means of calibration. The changes in blood volume and heart rate will also provide a measure of a subject's response, necessary for the quantification of the severity of the condition. Unlike arterial blood oxygen levels monitored by pulse oximetry, the oxygen debt incurred is measured when monitoring the venous side of the brain.

A low cost portable hypoxia monitor embodying the principles of the invention would be suitable for ambulatory patients, such as those suffering from a dysfunctional respiratory response in a range of pathologies, from emphysema, sleep apnea, severe asthma, SIDS or peripheral vascular disease. Sleep apnea is characterised by obstruction of respiratory airflow resulting in hypoxia which in severe cases can be life threatening. In infants, hypoxic-ischaemic injury is the most important cause of long-term neuro-development disability in newborn infants

requiring intensive care. (Studies of SIDS victims suggest that death may have been preceded by multiple episodes of non-fatal hypoxia. Some of the earliest work reported for non-invasive studies using near infrared spectrometer was on infants in respiratory distress).

Monitoring respiratory and cardiac responses to determine exercise tolerance in heart failure patients using ergometric bicycles or treadmills is well known. These tests can only be conducted under laboratory conditions which has little relevance to the routine daily exercise requirements of the patient. Further, not all researchers agree on the value of respiratory gas analysis in assessing exercise tolerance in heart failure patients but the measurement of peak oxygen uptake is reproducible and does provide some criterion of maximum exercise tolerance for heart failure patients. Exercise tolerance in heart failure is limited by peripheral circulation with the delivery of oxygen to the leg muscles. This is supported by evidence that muscle vascularity and biochemistry is more limiting in exercise than is cardiac output. Hence peripheral arterial-venous differentials may provide as suitable a marker of exercise tolerance as does respiratory gas status. As there is not a good correlation between exercise capacity and hemodynamics. Hence the exercise capability of the individual heart failure patient is not readily assessed in current laboratory protocols.

Given that heart failure patients have a marked decrease in physical activity due to their condition, one may expect a deconditioning of their skeletal muscles due to lack of exercise alone. In as much as under perfusion plays a part in deconditioning, there appears little evidence to suggest that it is a causative factor rather than a consequence of reduced exercise.

Heart failure patients generally have a very poor reactive hyperemia response, which is consistent with the impairment of the muscle vasculature's capacity to dilate. However, it has been demonstrated that an exercise induced increase in the reactive hyperemia response in trained leg muscles will also extend to increases in reactive hyperemia in other untrained (arm) skeletal muscle in sedentary subjects. The mechanism for this is unknown, but suggests that exercise has a systemic beneficial effect on peripheral blood flow rather than just a local response to exercised muscle. More importantly, there is evidence to suggest that submaximal long term exercise training is beneficial to the patient in stable heart failure in maintaining physical condition.

The use of near infrared spectroscopy in studies of exercise induced hypoxia in heart failure patients has shown that exercise intolerance of the heart failure subjects which results in exertion dyspnoea is due, in part at least, to the under perfusion of respiratory muscles during hyperventilation.

Hemodynamic studies provide little help in determining the safe functional capacity in heart failure patients. Supervised training in a laboratory setting while providing suitable monitoring of the patient's response to the training, is expensive and may involve considerable travel inconvenience for the patient. Also, a seldom considered problem with laboratory exercising is motivation. Treadmill walking or riding a stationary bicycle can lead to boredom very rapidly with loss of motivation. Rather, it would be preferable if the patient could perform the exercise of his/her choice in their own home or neighbourhood. This could be accomplished if a small portable device is worn during exercise that monitors and records hypoxia levels and respiration rates.

The literature suggests that diet modulates short term increases in endurance. These results are based on leg exercise data of an athlete in the supine posture in a nuclear magnetic resonance cavity. A more appropriate way of assessing dietary influence on performance would be to measure the rate of oxygen debt build-up under normal training conditions for that athlete. Motivational considerations may mask accurate laboratory results in exercise measurements requiring maximal exertion. Field exercise measurements would be more reliable. The near infrared spectrometer-signal could be obtained from individual large muscles such as the biceps and triceps brachii in the arms, adductor longus, gracillis, pectineus, vastus magnus etc in the legs.

Preliminary tests have shown that an exercise induced contraction of the flexor carpi muscles of the forearm produces a distinct deoxyhemoglobin transient commensurate with effort. Based on this alone, non-invasive monitoring of deoxyhemoglobin levels could provide important measurements to assess the performance of elite athletes. As an example, monitoring counter lateral muscles (on each limb) during training, could demonstrate poor symmetry of effort, which if present would reducing optimal performance. As mentioned for heart failure and respiratory dysfunctional patients, a device that measures deoxyhemoglobin, heart rate, blood volume changes and respiration simultaneously would have a place in sports medicine.

Recently it has become a practice for a coach to send an athlete for a muscle biopsy to determine fibre type content of relevant muscles. This information is desirable considering the balance between fast and slow twitch fibres is of primary importance in providing muscle power output and indurance. For instance, high oxidative slow twitch fibres predominate

in the leg muscles of marathon runners where work output must be sustained over long periods. In contrast, the readily fatigable but high power fast twitch fibres predominate in muscles used for sprinting. The determination of the fibre content using histology methods of the biopsied muscle is both expensive, and potentially flawed, as fibre distribution within the muscle can be heterogeneous. Hence there is no guarantee that the biopsied sample is representative of fibre distribution in the muscle overall. Further, these biopsies are not trivial, they involve the risk of infection, are painful and for large biopsies, can result in the muscle going into spasm for several days. Needless to say, these would be enforced rest days. Because of these factors, fibre typing is undesirable as a regular procedure.

When a muscle is electrically stimulated, the induced contraction causes a distinctive blood oxygen desaturation near infrared spectrometer signal. The rate of resaturation correlate closely with the proportion of fast/slow fibre type within the muscle. This finding has been shown with experiments conducted on sheep muscle in which the fibre distribution is known, semitendinosus, gastrocnemius, latissimus dorsi and the soleus muscles.

The aerobic threshold, which is a term used to describe a condition above which an athlete begins to build up an "oxygen debt", is a critical parameter for many athletes, such as marathon runners. For example, if too much energy is expended in the early part of a race, anaerobic reserves may be insufficient to allow the run to be completed. With cerebral monitoring, it can be ascertained at what work rate the deoxyhemoglobin ratio remains constant and under what rate (and environmental conditions) it begins to increase, signalling oxygen debt build up.

The stimulation of paralysed muscle is used in alleviating the secondary medical sequelae associated with the acute phase of rehabilitation in spinal cord injury (SCI). Low frequency electrical stimulation assists in reducing spasticity, deep venous thrombosis, decubitus ulcers, muscle atrophy and bone demineralisation in acute SCI individuals. Evaluation of changes in muscle condition may involves pre- and post-training assessment: CT scan, biochemical and histochemical assessment of lower limb muscle (muscle needle biopsy), to assess the effectiveness of the stimulation in restoring muscle tone. It will be evident that assessment of the therapy is extremely costly. Less evident, is the problems of implementation in muscle stimulation therapy. As the SCI patient has no feeling in the lower body, the level of transcutaneous electrical stimulation is assessed by the therapist by feel. That is, by qualitatively assessing the contraction induced in the muscle, by feeling muscle hardness.

A potential risk with this therapy is the possibility of over working a muscle. If the induced exercise by electrical stimulation drives the muscle into fatigue, then further stimulation could cause muscle damage. The effectiveness, or otherwise, of electrical stimulation therapy can only be assessed by histological/morphology studies of the biopsied muscles. The invasive nature of this procedure with the risks of infection make it unsuitable as a routine assay.

Using near infrared-spectroscopy, muscle blood oxygen saturation can be determined as previously described. The near infrared-spectrometer can also be used to obtain a relative measure of venous blood pooling. This can be obtained by measuring signal change with venous drainage when the leg is elevated. A relative measure of blood pooling in the veins of the

muscle results. The static state of the limb muscles in SCI individuals generally results in large venous pooling without therapy.

The muscle blood-oxygen desaturation can be measured with each induced contraction. Average tissue depth for detected photons is half that of the distance between the transmitting and receiving optodes.

Blood oxygen saturation monitoring is universally used during anaesthesia. This is done by pulse oximetry applied to the earlobe or finger. The limitations of this system when used for monitoring sleep apnea subjects is described above. While hypoxic events are less likely during most anaesthesia, monitoring the blood oxygen status of the brain is clearly more appropriate than that of peripheral tissue.

Under certain surgical procedures, significant desaturation can be expected, such as when the patient is placed on a heart-lung by-pass machine during open heart surgery. Under these conditions, a direct measure of brain blood oxygen desaturation by near infrared-spectroscopy would provide a distinct advantage over pulse oximetry monitoring of the peripheral tissue.

Even though low blood oxygen saturation is a major sign of sleep apnea, measurement of blood oxygen saturation via pulse oximetry provides little diagnostic value for reasons discussed above. Hence the necessity in monitoring the electrical output of the heart and brain (EGC and EEG respectively) to assess the effects of low blood oxygen desaturation. Ideally, measurements should be made of blood desaturation in the vital organs such as the brain or heart, and preferably of the venous blood draining the organ so that the true extent and duration of a hypoxic episode can be monitored.

Physiological responses such as increased blood flow to the organ should also be measured. As cardiac output will increase in response to decreasing blood oxygen levels to the vital organs. Hence reduced oxygen saturation can in part be compensated for by increased blood volume, increased flow rates and vascular bed dilation.

The method of near infrared spectroscopy of the invention will provide a non-ivasive linear measurement of blood oxygen saturation from 100 to 0% in brain and muscle. As well, the method also tracks changes in blood volume, respiratory rate and heart rate which will provide a measure of change in blood volume and flow in response to oxygen stress. This provides a quantitative measure of the hypoxia induced and a measure of the time course of the condition.

Unlike absorption in the visible region, carbon monoxide bound hemoglobin does not absorb the near infrared photons. Hence the high concentration of monoxide bound hemoglobin does not lead to errors in measuring the proportion of oxy-/deoxyhemoglobin content of the blood. Hence the inherent error in blood oxygen saturation measurements in smokers in pulse oximetry does not occur with near infrared-Spectroscopy.

SUMMARY OF THE INVENTION

According to one aspect of the invention there is provided a method for determining the absolute level of oxygen saturation in blood in deep tissue comprising the steps of:-

(i) irradiating a target area of tissue with radiation of at least two distinct wavelengths,

(ii) providing a first set of signals that represents the absorption of the radiation at each wavelength,

(iii) perturbating the venous blood volume in the target tissue,

(iv) providing a second set of signals that represents the absorption of the radiation at each wavelength after perturbation of the blood,

(v) subtracting the first set of signals from the second set of signals to provide a difference signal for each wavelength that represents the venous blood volume change as a consequence of the perturbation,

(vi) determining the ratio of the difference signals and comparing that ratio with the ratio determined *in vitro* to provide the absolute level of blood oxygen saturation.

The step of perturbating the venous blood in the target tissue may be carried out at constant metabolism or at changed metabolism and may be voluntarily hydrostatically induced, affected by venous occlusion, and electrically induced muscle contraction, arterial occlusion or voluntary muscle contraction.

Using a unique design for the optode assembly, brain oxygen is monitored continually from the sagittal sinus, the foremost cerebral region for venous blood draining the forebrain (centrally over the forehead above the eye brows). The optode assembly is held in place with a head band. Being placed over a hard surface (the skull), the optodes are less subject to measurement artefacts inherent with restless sleep. These movement artefacts are commonly observed with optode assemblies designed for finger or earlobe attachment. Also, being on the subject's forehead, the near infrared spectrometer optode assembly subjects the wearer to less discomfort and is less likely to be displaced during the night when held in position by the head band. In an alternate use, monitoring respiratory muscle, the optode assembly will be positioned in all subsequent

measurements, given the harness being fitted for exact and repeatable positioning of the assembly.

The optode assembly is connected via a flexible lead to a battery powered signal processing and storage unit. This unit is activated by a displacement strain gauge attached to the optode assembly headband. When the headband is stretched (placed on the subject's head) the unit is automatically activated to begin the blood oxygen saturation measurements. In the preferred configuration, an alarm is sounded if the tension in the strain gauge is changed from its an initial setting. Thus providing a warning to the user of dislodgment.

The near infrared spectrometer as a portable unit described in this application, is suitable for ambulatory use hence can be used for home diagnoses. A built in MODEM allows the user to send the night's monitoring to the clinic/medical centre for assessment. This procedure could be repeated for several nights with the results being sent to the clinic each morning. This method would have considerable advantage for initial assessment of sleep apnea in a subject, prior, during or post treatment with minimal inconvenience to the patient and more rapid and reliable diagnoses by the clinician.

To this point, no instrument has been capable of determining the proportion of fibre type in muscle. This currently requires invasive muscle biopsy and expensive and time consuming histology or protein analysis. The capacity of this invention to determine fibre type is there for unique. As is the capacity to monitor fatigue, electrical therapy and training.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic diagram of a near infrared Spectrometer having two laser diodes,

Fig. 2 is a schematic diagram of a near infrared Spectrometer having three light emitting diodes,

Fig. 3 is a schematic diagram of an experimental setup of a near infrared Spectrometer, power supply and display for *in vitro* assessment,

Fig. 4 is a graph of the deoxygenation of sheep red blood cells using the near infrared Spectrometer of Fig. 1,

Fig. 5A is a graph of the deoxygenation of sheep red blood cells as measured by the Spectrometer of Fig. 2 with a first pair of wavelengths,

Fig. 5B is a graph similar to Fig 5A with a second pair of wavelengths,

Fig. 6 is a graph showing the change in absorption of individual wavelengths as blood oxygen levels change,

Fig. 7 is a graph of the near infrared Spectrometer response to changes in blood oxygen in tissue with vessel occlusion,

Fig. 8 is a graph of the near infrared Spectrometer response to venous occlusion for relative resting arterial flow rate in the forearm represented as change in blood volume and change in deoxyhemoglobin,

Fig. 9 is a graph of the near infrared Spectrometer response to postural changes showing change in blood volume and change in deoxyhemoglobin,

Fig. 10 is a graph of the near infrared Spectrometer response to cerebral blood desaturation and blood volume perturbation with breath holding along with heart rate pulsatile flow,

Fig. 10a is a graph of relative absorption of radiation of two wavelengths during head tilt,

Fig. 11 is a graph of the near infrared Spectrometer response in respect of intercostal muscle showing desaturation and blood volume changes with respiration and breath holding,

Fig. 11a is an expanded region of the graph of Fig. 11 showing pulsatile blood flow,

Fig. 12 is a graph of slow fibre percentage for skeletal muscles compared with their expected slow fibre proportion,

Fig. 13 is a graph of the relative desaturation for isometic arm exercises,

Fig. 14 is a graph of the electrical pacing desaturation over a period of 5 minutes,

Fig. 15 is a schematic view of a headband for a near infrared spectrometer applied to a child's head,

Fig. 16 is a perspective view of a headband for a near infrared spectrometer according to one embodiment of the invention, and

Fig. 17 is a schematic diagram of a near infrared spectrometer according to one embodiment of the invention.

MODES FOR CARRYING OUT THE INVENTION

The near infrared spectrometer 10 shown in contains two GaAlAs laser diodes 11, 12 each capable of 20 mW optical power output. One laser diode 11 emits radiation at 813 nm while the other diode 12 emits radiation at 756 nm. In this instance there are two 756 nm laser diodes 12 each at 10 mW optial power which appears to be the highest power obtainable at or near this wavelength. Both laser diodes 12 are 'fired' together to produce the 20 mW optical power output. The laser diodes 11 and 12 are pulsed alternately by laser drivers 13, 14 and the levels of the photons reflected by tissue 55 at both wavelengths are compared using a signal from a 100 mm^2 silicon photodiode 15.

The output optical levels can be adjusted for the lasers, allowing the output optical power for both wavelengths to be matched. Photons received by the photo diode 15 for both wavelengths produce the same but opposite signal level, so that in the absence of differential absorption (ie. no deoxyhemoglobin) the signal level is minimal. However when absorption is greater at one wavelength than the other, a "difference" signal will be observed (756 - 813 nm).

The photo diode signal is amplified by amplifier 16 and fed to phase sensitive detector 17 which is also coupled to the laser drivers 13 and 14. The signal from the detector 17 is converted to digital form by the analogue-to-digital converter 18 and displayed on a computer screen 19. The laser drivers 13 and 14 are powered from a power supply 20 (± 5, 12 volts) through an oscillator 21 and respective diodes 22 and 23.

The near infrared spectrometer 40 shown in Fig. 2 uses three LED's (light emitting diodes) 41, 42 and 43 as photon sources and a 5 mm^2 photodiode 44 with an integral amplifier 45 providing the detector for photons reflected by tissue 55. The LED's are mounted as a cluster, 30 ± 10 mm from the photodiode, as will be described below.

The battery power supply 46 is connected to sequence timer 47 which is connected to the pulse power driver 48. The signal from the amplifier 45 is converted to a digital signal by the analogue-to-digital converter 49 and fed to the microprocessor 50 which is coupled to the 64K RAM memory 51, the sequence timer 47, the pulse power driver 48, keypad/display 52 and input/output 53. The LED's 41, 42, and 43 produce photons centred at 770, 790 and 850 nm respectively.

An experimental set up study of 756/813 nm signal levels over a range of hemoglobin oxygen saturation from 0 to 100% using the near

infrared spectrometer 10 of **Fig. 1**, converter 18 and display 19 and an *in vitro* sample being tested is shown in **Fig. 3**. The sample consists of an outer glass container 60 of milk, which provides a photon scattering environment simular to tissue 55. The inner glass 61 vessel contains 5% W/V aerobic yeast in a physiological buffer, again providing a highly scattering medium as well as an oxygen sink. Several drops of antifoaming agent control froth production when oxygen from supply line 62 is bubbled through the solution. The purpose of this solution is to act as a synthetic tissue sample that scatters and attenuates both the 756 and 813 nm photons in a similar manner to that in tissue. A measured volume of sheep red blood cells (RBC's) (previously washed in physiological saline) are then added and a magnetic stirring rod 63 used to keep the RBC's homogenously dispersed.

Oxygen is bubbled through the solution until the RBC's contain **100% oxyhemoglobin**. The optical power output of the lasers are adjusted to provide minimal signal level at 100% oxyhemoglobin, that is, the received optical intensities is the same for both wavelengths. The oxygen is turned off and over a period of time the oxygen is depleted in the solution by the oxidative metabolism of the yeast. This gradually displaces the oxygen from the hemoglobin and eventually produces RBC's containing **100% deoxyhemoglobin**. This procedure is monitored by the near infrared spectrometer 10.

Fig. 4 shows the "in vitro" calibration of the near infrared spectrometer 10 using 1.5% HcT of sheep red blood cells and 2% w/v of oxidative yeast. The deoxygenation of the RBC's was monitored by the near infrared spectrometer 10 with both blood volume (756 + 813 nm) and the hemoglobin desaturation signal (756 - 813 nm) is shown. The 600

mvolt change in signal level reflects the increasing quantities of deoxyhemoglobin with the yeast's removal of the oxygen. The almost constant signal level for blood volume, (the top trace in Fig. 4) shows that the isobestic point for hemoglobin under these conditions is a fraction less than 813 nm.

Figs. 5A and 5B relate to the "in vitro" desaturation of sheep red blood cells showing blood volume and desaturation signal levels and show the signal from the near infrared spectrometer 40 of Fig 2 in which LED's were used as a light source. Conditions are similar to that describes for **Fig. 4** above. In the first acquisition (Fig 5A) 770 and 850 nm were used as contrabestic wavelengths while 790 nm and 850 were used in the second acquisition shown in **Fig. 5B**. It is evident that 790/850 nm wavelengths give a better contrabestic pair than does 770/850 nm. Although obtaining an accurate contrabestic pair is not critical, providing the change in out put with desaturation change can be described in a formula.

For **Fig. 5A**, the spectrometer voltage range was 1300 m.V and for **Fig. 5B** the voltage range was 1026m.V.

Fig. 6 shows the change in the absorption of individual wavelengths from data from "in vitro" calibration of the near infrared spectrometer using 2.5% Hct sheep red blood cells and desaturating with aerobic yeast. The isobestic wavelength error at the 850 nm range was 170 m.volts and at the 790 nm range was 140 m.volts. The ratio of 140:170 (being 0.824) was used as a correction factor for the spectrometer when determining absolute oxygen saturation based on volume change data.

As can be observed in **Fig. 6**, as the blood oxygen saturation decreases, the 850 nm relative absorption decreases while that of 790 nm increases. That is, these wavelengths show an opposite response to blood

oxygen content. If they were accurate isobestic wavelengths then the signals will be equal but opposite. In this *in vitro* desaturation experiment blood volume remains constant.

The near infrared spectrometer measures relative absorption (in volts) from radiation at two wavelengths as back-scattered (reflected) from a target tissue. Absolute blood oxygen saturation is calcuated from measuring changes in blood volume at each wavelength. The blood volume change is achieved by movement of the target tissue relative to the heart, so inducing an adjustment in hydrostatic head. The absorption (voltage) change will be specific to each wavelength depending on the proportions of oxy-to-deoxy hemoglobin in the tissue.

For instance for a perturbation in muscle, and given blood consisting of 50% oxyhemoglobin, then the 850 nm voltage signal would increase (as oxyhemoglobin decreased by half) by the same amount as the 790 nm voltage decreased (as deoxyhemoglobin decreases by half). Providing that is, they were exactly isobestic wavelengths. A correction factor can be applied where they are not opposite-but-equal using a correction factor that corresponds to the difference in their voltage level that is determined by the *in vitro* calibration shown in **Fig. 6**. Note that there is only 60 nm difference between the two wavelengths. Hence their difference in response to volume change is only affected by their blood oxygen absorption characteristics. This will be independent of the scattering media, be it muscle, brain or artificial tissue used in the *in vitro* measurements. For accuracy, the desaturation (790 - 850 nm) relative absorption signal should remain approximately constant for both postural positions. That is, as the venous blood drains, the arterial vasculature responds to the lower pressure

by constricting to maintain vasculature resistance thus maintaining the same total vasculature arterial:venous proportions (25:72).

Having determined the total vasculature desaturation level, the venous desaturation level is obtained by multiplying by a correction factor of 0.96 as determined below. Again this is provided normal resting arterial blood oxygen saturation levels >95%. With continual monitoring, changes in saturation can be estimated by the relative changes in each wavelengths' absorption. So for a given increase of deoxy-, there will be a corresponding decrease in oxyhemoglobin relative absorption if this change is occurring on the venous side (increased metabolism), then the drop in the 850 nm signal will remain in approximate proportion to the increase in the 790 nm signal for a constant blood volume. But this relationship will not hold if it is occurring on the arterial side, as the proportions initial oxy:deoxy - proportions are ~24:1 in this vasculature.

Arterial dilation is inferred from increases in blood volume given a constant hydrostatic head. Hence an estimate of the change in arterial:venous volume can be used to modify deoxyhemoglobin distribution accordingly. This change would have to be an estimate as only the relative blood volume can be determined.

Given the desaturation estimate determined from the blood volume perturbation described above, further changes in relative absorption from the measured level can be inferred from the near infrared spectrometer calibration. That is, given that the desaturation slope has been determined *in vitro* (for the near infrared spectrometer) then the initially calculated saturation percentage lies on a straight line of known slope (volts/%-saturation) as shown in **Fig. 4**.

Hence the spectrometer can provide a voltage signal that with instrument calibration and blood volume perturbation, a measure of blood oxygen saturation is obtained.

The spectrometer can also measure relative blood volume by changes in 790 + 850 nm relative absorption in volts.

The proportion of slow:fast fibre in muscle can be determined from the desaturation relaxation slope of a contracting muscle.

A number of experiments were conducted to ensure that the near infrared spectrometer [10 or 40] responded to changes in blood oxygen in tissue exclusively. This was achieved by using a blood pressure cuff to occlude the blood flow to the forearm. This is done by placing the cuff around the upper arm (above the elbow) and pneumatically applying a pressure of 220 mm Hg (supra-systolic). The forearm was maintained in a horizontal posture with the spectrometer optodes placed adjacent to the muscular region (over the brachioradialis and extensor carpi radialis longus muscles) of the forearm.

With vessel occlusion, the only changes in the forearm can be attributed to muscle metabolic activity. This can be observed in **Fig. 7** which shows the near infrared spectrometer response to occluded forearm and release. With the initial forearm occlusion (point I) applied for five minutes. In this time, the oxyhemoglobin reaches their minimum level in the muscles' vasculature. This will desaturate the pooled blood in the muscle arterioles and capillary bed (and probably the venules) thus maximising the proportion of deoxyhemoglobin present.

When the occlusion is released (point II) reactive hyperemia (RH) occurs (point III), the (hypoxia induced) dilated vasculature will allow oxygenated blood flow through to the venous side. If the cuff is reapplied

at the high point of reactive hyperemia (point III), a high level of oxyhemoglobin is trapped in the muscle vasculature. However, the lack of blood flow increases the metabolite content of the muscle after five minutes which switches off oxidative metabolism (in most subjects) so that when the cuff is again released (point IV), there is some seconds delay in the resumption of metabolism until the metabolites have been removed from the tissue. During this time the capillary and venous vasculature are flushed out with arterial levels of oxyhemoglobin.

The result of this double occlusion is observed in **Fig. 7** where at the peak of reactive hyperemia (point III), the arm was again occluded for a further ten minutes before the cuff was again released (point IV). Blood oxygen saturation with the first occlusion (point III) was well below that for the second occlusion (point V). It is evident from this figure that arterial levels of oxyhemoglobin were only achieved after the second occlusion. Hence for each subject, a maximum deoxyhemoglobin content (within five minutes of the first occlusion) and a minimum deoxyhemoglobin content (within 20 seconds of the release of the second occlusion) can be calibrated. Similarly maximum blood volume content of the measured region corresponds to that observed after the release of the second occlusion. Given different skin pigment, fat content and possibly other factors, calibration has to be conducted on each subject in order to obtain base line values for deoxyhemoglobin levels and blood volume.

Fig. 8 is a graph of the near infrared spectrometer response to venous occlusion for relative resting arterial flow rate in the forearm represented as change in blood volume in the top trace and change in deoxyhemoglobin in the bottom trace.

A blood volume signal change is observed with changes in posture. Blood volume with postural changes are well documented in the literature, having been assessed by limb Plethysmography (volume change measurements). Using near infrared spectroscopy, not only can the relative volume change, be monitored, but the vasculature response is also measured. **Fig. 9** shows blood volume decrease in the forearm of a subject where the arm position is lifted from the waist to shoulder level. This represents a change in hydrostatic head (referenced to the heart) of some 30 centimetres. This large change in volume results from the reservoir capacity of the venous vasculature. As the arm is raised, blood drains into the trunk reducing blood volume in the limb. It can be observed that the desaturation signal (bottom trace) shows transient changes which correlate to the vascular adaptation to the rapid change in hydrostatic head. The timing for these transients are under neuromuscular control. The rate of blood volume recovery after the forearm has been returned to the initial position we suggest is determined by arterial flow.

Similar signal attributes are observed with hydrostatic changes when monitoring brain during changes in posture. This shows that by measuring the postural changes with near infrared spectroscopy, it is possible to obtain a relative measure of:-

i) venous drainage,

ii) neurovasculature response times and

iii) arterial flow rates to the muscle.

It will also be shown, absolute measures of blood oxygen saturation are obtained using these volume perturbations.

Conversions of near infrared spectrometer signals from proportions to absolute blood oxygen percentage is currently estimated by weighting

the attenuation of intercepted photons received for two or more specific wavelengths. These have been determined empirically from measurements on phantoms or measurement of arterial-venous differences by conventional blood gas oximetry (obtained from venous and arterial samplings) and comparing these measured levels to near infrared spectrometer readings at the various wavelengths which are then weighted to obtain the best fit. Directly using the Beer-Lambert relationship for absorption is not practical as the photons received have an unknown path length due to scattering. This can be allowed for by determining average path length using time of flight measurements of photons through brain tissue and muscle. To obtain an estimate of path length by multiplying the distance between the optodes by a path length factor that accounted for the expected average scattered path. Although this is currently used for obtaining blood oxygen desaturation values, no allowance is made for changes in the vasculature during oxygen stress. So that an approximation of venous blood oxygen levels is not accurately obtained.

The assumption taken by most investigators that near infrared spectrometer provides a signal that corresponds to the venous saturation levels is only adequate under resting conditions with high arterial blood oxygen saturation. Errors in this assumption occur under arterial oxygen stress conditions. Criticisms of continuous wave near infrared spectrometer accuracy's are mainly due to the algorithms' incapacity in allowing for changes in vasculature volume and changes in desaturation on the arterial side of the vasculature as will now be demonstrated below where:-

W = whole blood volume

W_{Hb} = whole deoxyhemoglobin blood volume

W_{HbO2} = whole oxyhemoglobin blood volume

A_{Hb} = deoxyhemoglobin proportion in the arterial system

A_{HbO2} = oxyhaemoglobin proportion in the arterial system

V_{Hb} = deoxyhemoglobin proportion in the venous system

V_{HbO2} = oxyhemoglobin proportion in the venous system

C_{Hb} = deoxyhemoglobin proportion in the capillary bed

C_{HbO2} = oxyhemoglobin proportion in the capillary bed

It has been postulated that the cerebral blood distribution is: arterial 25%, venous 72% and capillary 3%. Under resting conditions and normal cardiac and lung function, arterial saturation can be taken as is 98% and cerebral venous saturation around 65%, the saturation in the capillaries is generally taken to be between the artery and venous levels in this case, 82%. Then it follows that the deoxyhemoglobin levels are 2%, 35% and 18% for the arteries, veins and capillaries respectively.

From equation 1:-

$$W_{Hb} = (100 - 98\%)A_{Hb} + (100 - 65\%)V_{hb} + ([2 + 35]/2)C_{Hb}$$

$$= .25x.02 + .72x.35 + .03x.18 \text{ (total proportion of Hb)}$$

$$= 0.005 + 0.252 + 0.005$$

$$= 0.262 \text{ (or 26.2\% deoxyhemoglobin in the tissue vasculature)}$$

It follows that the oxyhemoglobin is $W - W_{Hb} = 1.0 - 0.262 = 0.738$

From equation 2:-

$$W_{HbO2} = 98\% \times A_{HbO2} + 65\% \times V_{HbO2} + 82\% \times C_{HbO2}$$

$$= 0.245 + 0.468 + 0.0246$$

$$= 0.738 \text{ (or 74\% of blood volume consists of oxyhemoglobin)}$$

It will be evident that the bulk of the deoxyhemoglobin is in the venous vasculature:

$$V_{Hb}/W_{Hb} \times 100 = 0.252/0.262 \times 100 = 96\%$$

While ~2% (0.005/0.262x100) of the deoxyhemoglobin concentration is found in the arteries of the brain. A similar figure can be derived for deoxyhemoglobin distribution in muscle also.

The deoxyhemoglobin signal using equation 3 is:

$$W_{Hb}/W = W_{Hb}/(W_{Hb} + W_{HbO2}) \times 100 = 26.2\%$$

Given that the contrasbestic signal (790nm - 850nm) measurement is representative of W_{Hb}/W, the near infrared spectrometer measurement should be multiplied by 0.96 to obtain the venous blood deoxyhemoglobin proportion. The contrabestic wavelength is close to 790/850 nm as can be seen in Fig 5, where only a small error in blood volume was found over the full range of blood oxygen desaturation.

There would be differences in individuals for the values used here, such as arterial deoxyhemoglobin levels of 5% (rather than 2%) or venous deoxyhemoglobin levels of 30% (rather than 35%). But the venous proportion under these conditions is still above 0.9. Thus nearly all the near infrared spectrometer desaturation signal can be attributed to the venous blood oxygen desaturation level.

It is likely that the high correlation of invasive venous blood gas sampling measurements with that of near infrared spectrometer measurements has led investigators to assume that the near infrared spectrometer difference signal arises from the venous side only. But our analysis shows that this is a misinterpretation and that the difference signal represents the deoxyhemoglobin signal for the total blood volume. This

would be of little consequence if it were not for the shift in blood volume and deoxyhemoglobin levels in the arterial blood during oxygen stress.

For example, given even mild levels of desaturation in the arterial vasculature, such as that represented in short breath holding periods. It is no longer true that the signal is representative of venous desaturation.

Fig. 10 is a graph of the near infrared spectrometer response to cerebral blood desaturation and blood volume perterbation with breath holding along with heart rate pulsatile flow. With breath holding, the arterial blood begins to desaturate (top trace) and the build up in carbondioxide causes the arterial vasculature to dilate resulting in increase in measured blood volume as shown in the bottom trace. The oscillations in the graphs of **Fig. 10** are due to pulsatile flow corresponding to heart rate.

For instance, by expelling air from the lungs then not breathing for twenty seconds can reduce arterial saturation from 98% to 88% (measured in the skin by pulse oximetry). In response to this mild oxygen stress, there is a decrease in the oxygen gradient from capillaries-to-tissue hence a slight decrease in oxygen transfer occurs. So that the arterial-venous difference would decrease from 33% (98 - 65) to around 30% (88 - 58). As can be seen in the bottom trace of **Fig. 10**, blood volume increases. This is in response to the build up of carbon dioxide in the blood. That is, the arterial vasculature dilates increasing arterial blood volume from 25 to an estimated 35% of the total vasculature.

Recalculating the deoxyhemoglobin distribution under these conditions is as follows:

A_{HbO2} = 88% after 20 second breath holding

V_{HbO2} = 58% " " "

C_{HbO2} = 73% ie. mid arterial-venous levels

new volume - arterial = 35%, venous = 55% and capillary = 6%

(increase flow will maximise capillary recruitment to around X2)

Hence the distribution of deoxyhemoglobin can be derived as follows:

(0.88 X 35%) = 7.7% arterial deoxy. proportion

(0.58 X 72%) = 23.1% venous " "

(0.73 X 6%) = 1.6% capillary " "

Total deoxyhemoglobin proportion is .077 + .231 + .016 = 0.324

Hence due mainly to changes in the arterial vasculature, the near infrared spectrometer signal corresponding to $Hb/(Hb + HbO_2)$ increases to 0.324 of the maximum signal. However, only ~71% of this signal change is attributable to the deoxyhemoglobin levels in the venous vasculature under this condition. To ignore these physiological changes with oxygen stress results in nearly a 30% error (from 96% to 71%) in estimating venous saturation levels. During hypoxia total blood volume can change from 25 to 48% of total volume. The proportion of deoxyhemoglobin increase in the arterial vasculature can result from a reduced cardiac output or else pulmonary dysfunction. It may also increase with during vigorous exercise. It will most certainly increase during air flow obstruction as is experienced during sleep apnea.

The error introduced by increased capillary volume can be neglected due to its small volume as well as low hematocrit.The hematocrit (% hemoglobin in the tissue or blood) of the arterial and venous blood is about 45%, whereas in the capillaries it is approximately 10%. This is caused by a differential speed of the red blood cells and the plasma going through the capillaries. Hence the 3% blood volume measured for the capillaries is likely

to be an over estimate given that the main consideration is hemoglobin content of the vasculature.

Arbitrarily less than 80% arterial blood oxygen saturation may be regarded as hypoxia. Levels below 50% arterial blood oxygen may occur with sleep apnea. Under these conditions, carbon dioxide build-up induces a physiological response for increased blood flow in the brain.

Resistance to blood flow is in the small arteries, so that the flow increase results from their dilation. This increased dilation is recorded by near infrared spectrometer as an increase in blood volume. So with extreme hypoxia, the arterial volume could increase to 48% of the blood volume (from 25%). This increase is due entirely to an increase in the arterial volume so that it can be used to index the changing proportions of arterial to venous vasculature. The capillary bed volume will also increase, however, considering its small contribution to whole vasculature ~6% fully dialated, as well, the hemoglobin content is lower than this value suggests due to the proportionally low hematocrit, one fifth of that of the arterial vasclature. So the capillary bed's contribution to total hemoglobin can be ignored. Hence an algorithm for determining venous blood volume proportions under hypoxic conditions can be derived by measuring the proportional change in hemoglobin signal attenuation.

Several studies using near infrared spectroscopy have shown that the estimate of blood oxygen desaturation of the brain correlates well with the venous blood desaturation. Based on the venous blood deoxyhemoglobin near infrared spectroscopy correlation it has been concluded that the infrared photons detected were mostly, if not entirely, from the venous vasculature.

However, as demonstrated above with calculations of the deoxyhemoglobin distribution in the brain vasculature, the correlation of the deoxyhemoglobin proportion with the venous vasculature can be explained by the deoxyhemoglobin distribution within the vasculature when at rest. Not recognising the cause of the venous blood deoxyhemoglobin correlation will lead to unacceptably large errors when increases in arterial proportion of deoxyhemoglobin occurs.

For instance, if the detected photons were from the venous side only, then no error would be expected with a blood volume proportion shift to the arterial side during hypoxia as the venous deoxy-/oxyhemoglobin ration measured would remain unaffected. Nor would the signal's accuracy be compromised with increasing arterial desaturation, again because it is 'only the venous vasculature being measured'. But if, as is contended in this specification, photons traverse the total vasculature, then changes in vasculature blood volume and arterial desaturation must be accounted for in order to obtain accurate measurements of venous desaturation.

Evidence that the photons traverse the whole vasculature is implied in the graphs of **Fig. 10a** which show the change in cerebral blood volume at 2 isobestic wavelengths during head tilt. Pulsatile flow is more evident at the 850 nm wavelength which is in response to systolic-distolic changes on the arterial side of the vasculature. These signals were obtained non-invasively from brain with posture induced perturbations. Pulsatile flow is evident for the 850 nm wavelength, which is more responsive to oxyhemoglobin. Pulsatile flow is only present on the arterial side of the vasculature. This pulsatile flow is even more evident in **Fig. 10.**

These results have been verified on a number of subjects while simultaneously measuring the pulse rate to establish that these cyclic

pulses are synchronous with pulsed cardiac output. The amplitude of these pulses leaves little doubt that they are from arterial pulsatile flow, little if any pulsatile flow occurs on the venous side of the vasculature.

The volume and hematocrit of the capillary bed make it an unlikely source of such large pulses given the low concentration of capillary hemoglobin. These results are totally inconsistent with the claim that the received photons are coming from the venous vasculature. They are consistent for there being a significant proportion of the signal arising from the arterial vasculature.

As can be seen in **Fig. 10a** the photons detected do not arise only from the arterial side as is demonstrated by a change in signal strength with a change in posture. Such a drop in blood volume correlates to a change in hydrostatic head - change in pressure height with respect to the heart. This is a well known phenomenon described in the literature using plethysmography (volume change) studies. These static head changes are confined to the venous side of the vasculature, although they are generally accompanied by arterial changes in blood volume so as to maintain a constant desaturation rate.

Hence, these results give strong support to our claim that photons traverse the whole vasculature and that the conclusions of other investigators that the near infrared spectroscopy signal correlates with the venous deoxyhemoglobin levels are only correct under specific conditions.

In **Fig. 8**, the blood volume and desaturation signals are shown. These were acquired while the optode assembly was placed on the forearm over superficial muscle with the arm being moved from waist to shoulder height. The increase in signal level was caused by venous blood drainage from the arm due to the change in hydrostatic head. In response, the

arterial vasculature constricts to maintain appropriate pressure, hence the desaturation signal shows little change.

With this volume change, the 770 nm signal adjustment will be dependent on the extent of volume change and the proportion of deoxyhemoglobin in the blood volume being measured. The change in the 850 nm signal will likewise reflect, the extent of volume change and the proportion of oxyhemoglobin in the blood volume. As their response to volume change will be the same, the differential change between these wavelengths can be subscribed to the deoxyhemoglobin:oxyhemoglobin ratio.

For instance, if the oxyhemoglobin content was 60% of total blood volume, then by decreasing the blood volume, the 850 nm signal will be more influenced by the change than will the 770 nm signal which is more strongly influenced by only 40% of the blood volume (the deoxyhemoglobin). Hence the extent of their differential change will reflect the proportion of saturated blood in the volume changed. Providing that is, the vasculature proportions remain constant, which means that the desaturation signal is unchanged.

With the set of optodes used, the *in vitro* measurement for the wavelengths in the experiments of **Fig. 5**, showed that the 770 nm signal changed 8.8 mV/1% in blood oxygen saturation whereas the 850 nm signal changed 5.1 mV/1% saturation (the 790 nm signal changed 5.6 mV/1% saturation).

So that for a change in blood volume which consisted of 50% deoxyhemoglobin, the ratio of the change in 770nm:850nm will be 8.8mV:5.1mV, which is a ratio of 1.7255.

Signals acquired from blood where the deoxyhemoglobin is less than 50%, the ratio 770:850 nm will be <1.7255 or when the deoxyhemoglobin proportion is greater than 50% then the ratio will be >1.7255. Based on the change in oxy:deoxy proportions, the ratio of 770nm:850nm absorption with the blood volume thus allows the calculation of the % blood oxygen saturation in the tissue, based on blood volume perturbations.

A plot for a range of these proportions is shown in **Fig. 6**. The slope of the line of best fit (r^2) corresponds to the formula Y = 60.755 + - 45.405xlog(X) where Y = %-saturation and X = 770nm/850nm ratio. The latter is obtained from the near infrared spectrometer measurement.

Using a blood volume perturbation similar to that of **Fig. 9** the following results were obtained:

Table 1

wavelength	waist height	shoulder height	difference	770/850 ratio
770 nm	0.150 volts	0.267 volts	- 0.117 volts	
850 nm	0.237 volts	0.352 volts	- 0.115 volts	1.017
770 - 850	0.135 volts	0.132 volts	0.003 volts	

From **table 1**, X = 1.017, so from the formula above, Y = 65% blood oxygen saturation in the resting forearm of this subject. For a venous saturation estimate Y is multiplied by 0.96. As can be seen in the table above, the desaturation signal indicated that the oxy:deoxy proportions remained constant with the change in hydrostatic head change hence no adjustment to the calculated saturation need be made. Data gathered for eighteen subjects in this manner gave an average blood oxygen saturation of 57% (range 48 to 88). This compares to deep venous blood sampled in

the forearm of 12 subjects at rest that gave an average saturation of 53% (range 39 to 81). Adjustments to the saturation need to be made when the desaturation signal changes significantly with the postural change.

The same method for obtaining saturation levels can be obtained from the brain using a head tilt to pertubate the blood volume as shown in **Fig. 10a.**

Cerebral Blood Oxygen Monitoring

The brain is the most vascularised tissue with a hemoglobin content of about 150 μmole (in the brain vascular bed). The distribution of the blood volume in the vascular system is as follows: 25% arterial, <5% capillary (there are studies that show this may be as low as 2.8% at rest) and 72% in the venous vasculature. With normal respiratory and cardiac function, the arterial blood oxygen saturation is 98%. Whereas the venous blood oxygen saturation in the brain is around 65% due to brain oxygen extraction. The capillary bed is generally assumed to be mid way between these two saturation levels, ~80%. Hence the distribution of deoxyhemoglobin is: 2% arterial, 2% for the capillary bed (or less) and 96% for the venous vasculature. Hence under normal conditions the near infrared spectrometer signal appears to arise from the venous vasculature. Even in hypoxic conditions where the arterial side has reduced oxygen saturation, the difference signal mainly reflects the venous blood oxygen saturation levels. At the end of a hypoxic episode, the arterial blood rapidly returns to 98% saturation so that the desaturation signal again is representative of the venous deoxyhemoglobin levels, thus providing accurate monitoring for the time of normal arterial blood oxygen saturation levels in the brain. In practice, a hypoxic event results in an oxygen debt.

So that even though normal arterial saturation levels may quickly return, the venous saturation level may stay depressed for some time.

In the near infrared, bone is a scattering medium with only limited amounts of absorption. The skin overlying the cranium has proportionately low blood volume levels compared to grey matter, so that an optode assembly placed over on the forehead produces a desaturation signal whose attenuation is influenced mostly by the brain's vasculature. Signal changes due to saturation of blood volume changes can be attributed almost exclusively to the brain's vasculature. The sagittal sinus, located in the forebrain lob region, contains the venous vasculature draining some 80% of the forebrain.

Fig. 10 shows near infrared spectrometer monitoring of the forebrain region during short term breath holding for both desaturation and blood volume. After twenty seconds of breath holding the deoxyhemoglobin level changes show the effects of mild arterial desaturation. In sleep apnea, breathing commonly stops for up to one or more minutes.

The bottom trace in **Fig. 10** shows changes in blood volume during twenty seconds of breath holding as well as relative changes in cardiac output. The blood volume increases in response to carbon dioxide build up. This blood volume will help compensate for the reduced blood oxygen content and its extent probably varies person-to-person . Similarly, the cardiac output response (increase heart beat rate), along with vessel dilation would provide diagnostic information as to the subject's physiological response to a hypoxic event.

With heart failure, both parameters could be compared to a level programmed into the device and an alarm set off if the tissue hypoxia or respiration rate exceeds these levels, warning the patient to rest or

terminate the exercise. If the device had an inbuilt MODEM, the stored information could then be down loaded to a clinic or hospital computer for analysis by a clinician.

An assessment on the progress of the patient's training could in part be made based on the level and extent of the patients deoxyhemoglobin levels, changes in blood flow, heart rate and respiration rate for the training protocol. Depending on the signal level and where the measurement is made, the pulsate blood flow that corresponds to heart rate is obtained see **Fig. 9**, expanded region in the bottom traces. The respiratory rate can be obtained from the pulsatile respiratory flow shown in **Fig. 9**, top traces.

Figs. 11 and **11a** are near infrared spectrometer traces taken from respiratory muscles in which both the respiratory desaturation of the intercostal muscle and the heart pulsatile flow are clearly observed. Based on the analysis of the near infrared spectrometer output of the exercising heart failure patient, alterations to the exercise regime could be suggested by the clinician. While not substituting for patient-doctor contact, it would provide an intermediate level of patient monitoring in a training protocol which would be more cost effective and convenient to both the patient and clinic/hospital resources.

Fig. 12 shows the percent slow fibre obtained from near infrared spectrometer measurements for skelatal muscles compared with their expected occurrence with the semitendinosus used as a dependent variable. The expected occurrence was based on histological assessment. The other three muscles - latissimus, gastroc and soles - show calculated slow fibre proportions that were close to that expected. This is the only non-invasive method for fibre determination in muscle. The rapid desaturation relaxation signal can also be obtained in brief voluntary

isometric contractions by subjects rather than relying on electrical stimulation.

Assessment of fatigue is generally subjective so that the ability to monitor the rate of deoxyhemoglobin build up is an advantage as a method of assessing fatigue. Fig. 13 shows the build up in deoxyhemoglobin in a near infrared spectrometer signal on contracting forearm muscle. Each trough is associated with a contraction, with a general increase in deoxyhemoglobin levels indicated by the dotted line. The slope of this line can provide a measure of fatigue onset.

We have found a 30 mm optode separation to be suitable for acquiring photons from superficial muscle in humans. A band with the optodes is strapped appropriately to the limb(s) under therapy. The desaturation signal can be displayed on a computer screen in real time, allowing the therapist to assess the fatigue state of the exercising muscle. If the rate of induced contraction exceeds that which the muscle can sustain, the desaturation signal will at each contraction will decrease. The onset of fatigue is hard to assess as the subject lacks pain feed back. Also the muscle will continue to contract under non-oxidative metabolism so the therapist can be unaware of the fatigued state.

Fig. 14 shows 3 blocks A, B and C of a graph which demonstrates the effects of near infrared spectrometer monitoring a paraplegic subject during isometric contractions for five minutes (at 2 seconds stimulation followed by 2 seconds relaxation. The lower trace in each block shows the blood volume response. The upper traces show the induced desaturation decreasing such that by four minutes no specific oxygen extraction with stimulation was observed. The relative deoxyhemoglobin level rose 500 mV

(corresponding to approximately 50% increase in deoxyhemoglobin for the calibration used).

Using near infrared spectrometer, the therapist is able to adjust the voltage level of the stimulator down to a level where the desaturation signal continues to show oxygen extraction at each contraction. That is, the muscle will not be driven into fatigue with extended time of electrically induced exercise with glycolitic metabolism. To this point in time, no method other than the therapist's "feel" is used in this type of muscle therapy.

One method of calibrating the near infrared spectrometer for the individual subject, would be to measure blood volume change in specific muscles with leg elevation and calculate the muscle blood oxygen saturation as previously explained. A double cuff determination of the 98% saturation signal level, also previously explained, see Fig. 7, would then provide two points along a linear desaturation signal from which the absolute desaturation level could be measured for that muscle.

Vascular tone can also be assessed by the extent and time course of reactive hyperemia as seen in Fig. 7. Reactive hyperemia, correlates well with vessel dilatory response. These measurements would be repeated at intervals during therapy. The basal rate of oxygen consumption will change with changes in muscle mass, capillary bed and/or oxidative metabolism. That is, the muscle hematocrit (% hemoglobin) will increase to accommodate muscle transformation to a more oxidative metabolism that occurs with electrical stimulation of muscle. Hence the effectiveness of the therapy can be quantified which will provide information to assess the level of stimulation required to maintain muscle tone. Hence the effectiveness of

the therapy can be quantified which will provide information to assess the level of stimulation required to maintain muscle tone.

As the induced venous blood-oxygen desaturation peak is a measure of muscle oxygen consumption (obtained by measuring the area under the desaturation peak), and as oxygen consumption provides a measure of skeletal muscle power out put, a relative measure of muscle power could be measured by near infrared spectroscopy. Hence the quantification of the muscle condition can be used to assess the suitability of the muscle for appropriate stimulation in lower limb mobility by induced contractions.

During the initial electrical stimulation, the near infrared spectroscopy optode-band will be strapped to the limb to monitor the rate of increase in the blood-oxygen desaturation signal. The level of stimulation will be reduced if the near infrared spectrometer's signal indicates a capillary blood-oxygen saturation approaching ~5%, as it is possible that tissue damage would be sustained if the stimulation continued for a length of time with the muscle in an hypoxic state. It is anticipated that effective training will increase muscle fatigue resistance. near infrared spectroscopy will provide continual assessment on the effect of the training program on improved muscle tone and at what rate these changes are occurring.

The attributes of muscle fibre type can also be assessed as part of near infrared spectroscopy monitoring in the methods previously discussed under "sports medicine use of near infrared spectrometer". Similarly the algorithms for determining the resting levels of blood oxygen saturation could be applied.

A near infrared spectrometer according to one embodiment of the invention is shown in Figs 15 to 17.

The transmitting optodes, that is the light emitting diodes (LED's), 41 (790 nm), 42 (850 nm) and 43 (770 nm) are mounted on thin copper etched board 60 encased in silicon rubber impregnated with carbon black. The receiving optode, that is the photodiode 44 is similarly mounted on a thin copper etched board 61 encased in silicon rubber impregnated with carbon black. Transparent silicon rubber is placed over the optodes 41, 42, 43 and 44. The optode assembly 64 is attached to a elastic/velcro band, 62. which also carries a displacement strain gauge 63 whose action and function is explained below.

The elastic/velcro band 62 is placed around the head as shown in **Fig. 15** with the optode assembly 64 positioned over the forehead of a subject in order to measure cerebral blood-oxygen and blood volume changes in the forebrain region. The skin and bone of the forehead provide little attenuation to the near infrared photons compared to that of the hemoglobin in the sagittal sinus, the foremost cerebral region with venous draining of the forebrain.

The strain gauge 63 is a flexible linear displacement capacitive strain gauge which acts like a variable capacitor when stretched. The strain gauge 63 is connected to a capacitance-dependent oscillator circuit 65 to provide a change of frequency upon change in its length.

The oscillator circuit 65 is connected to a frequency-to-voltage converter circuit 66. The strain gauge 63 will provide a voltage signal (or frequency signal) which will change if the head band 62 is displaced from its initial setting. The frequency could be time interval sampled by the microprocessor 50 to obtain the strain gauge tension if microprocessor power-down requirements are not used - in which case only the CMOS 555 timer IC is required).

When the head band 62 is stretched further than its resting level, the strain gauge 63 provides a change in voltage which changes the state of a comparator and activates a gate of a MOSFET-transistor 67 whose source/drain controls power from battery 68 to the near infrared spectrometer circuit. Hence the spectrometer is activated by the placement of the head band 62 so that battery drainage is curtailed automatically when the subject removes the headband 62. The 128K RAM 69, MODEM 70 and LCD display 71 are powered independently of the near infrared spectrometer circuit.

The other function of the strain gauge 63 is to provide a base line out put which represents a specific position of the head or limb band 62. Any movement of the band will usually lead to a different tension on the strain gauge 63. Hence when the initial out put voltage of the strain gauge 63 is coupled to an alarm 72 via EPROM 73, a significant change in the head/limb band position will set off the alarm 72. This would be an important feature in SIDS monitoring where it would be essential to alert the carer if the band 62 is displaced from the head of the infant. It also provides a convenient feature to assist the repeat placement of the head/limb band for repeatable measurements. Asymmetry of the limbs (and the head to a lesser extent) means that the previous position of the optode assembly could be determined by orientating the band until the voltage level of the strain gauge was the same as previously obtained.

The LED's 41, 42 and 43 are fixed to a PC fibre glass board, 17 X 6 mm, and their leads placed through holes and soldered to the etched copper contacts on the reversed side of the board. The cathode of each LED 41, 42 and 43 is soldered to a common contact (ground) while the anode of each is connected to a multi stranded insulated conductor. A

similar approach is taken for the attachment of the photodiode 44 to a 5 X 5 mm PC board. The diode 44 consists of a 5 mm^2 surface area diode in a hermetically sealed metal package with an incorporated amplifier. Again multi stranded insulated connectors provide negative and positive terminal plus ground (reference) and output. Except for the glass window, the photodiode with its cabling are encapsulated in silicon rubber. The LED and photodiode optodes are attached to cloth, 30 ± 10 mm apart as shown in **Fig. 16.**

To provide low cost, robust and low power for portability, the infrared light source for the near infrared spectrometer comes from three gallium-aluminium-arsenide light emitting diodes (LED's) manufactured to emit light in the wavelength ranges of: 760 ± 20 nm, 800 ± 20 nm and 840 ± 20 nm. Each of these wavelength range LED's provide a peak optical power output of 40 mW with a rise time of less than 20 ns. While these LED's draw 200 mA to obtain 40 mW radiation output, their fast rise time makes it possible to design a circuit with short duration pulse output, duty cycle of <2%. This reduced the average power output to approximately 30 milliamps average continual usage, which is suitable for battery power.

While in theory only two light sources are required (760/805 nm), acquiring a signal either side of the isobestic wavelength (805 nm) is used here because of the broad wavelength emission band of the LED's (±20 nm). Thus in a worse case match, a 780 nm LED (760+20 nm) could be matched with a 780 nm (800 - 20 nm) which would not produce a differential signal for deoxyhemoglobin. Nor would any close combination of these wavelengths produce a differential signal of sufficient signal amplitude. However, worse case condition for the approximate contrabestic

wavelengths, 760-to-850 nm would result in sufficient wavelength separation (780 to 830 nm) so that a differential deoxyhemoglobin signal would be observed.

The third wavelength 800 ± 20 nm is close enough to the isobestic wavelength (between 805 and 815 nm), to provide a compensatory signal to monitor blood volume changes. Each set of LED optodes would be tested to include a suitable algorithm to compensate for wavelength emissions that deviate from 770/800/850 nm ideal.

As shown in **Fig. 17**, an oscillator triggers the sequential illumination of the light emitting diodes (LED's) 41, 42 and 43 housed in optode assembly 60 directly over the tissue being measured. The LED drivers 48 provide the synchronised timing signal to enable the 4 channel analog input to the data acquisition IC.

The photodiode 44 is positioned 30 ± 10 mm from the cluster of LED's, and captures a proportion of the diffused and scattered photons returning from the tissue. The photon induced electric current is amplified. Simultaneously, a channel of the data acquisition IC is enabled to receive the amplified voltage derived from the photon back scatter from tissue of the LED illuminated. A sample-and-hold circuit within the data acquisition IC stores the voltage which in turn is converted to a digital signal and placed at the data acquisition's output registers onto an eight bit bus. This detection, storage and conversion occurs sequentially for each LED illuminated for each cycle of the oscillator. Data is stored from the four channels in blocks in static RAM 69.

Fig. 17 also shows the use of a CMOS-microprocessor 50 with 1K EPROM included that will allow software control settings to be programmed into the microprocessor. This will include storage protocol of

the acquired data, the capacity to detect an out-of-range measurement (based on preset levels) and activate an alarm, provide a software protocol for MODEM transmission of the stored data as an ASCII file format as well as a keypad and numeric liquid crystal display for parameter settings.

The microprocessor and data acquisition IC's have power down capability, hence their main power requirements will be restricted to a narrow window (50μs) in the cycle. The date acquisition IC channel enable sequence including that for the strain gauge. The free running oscillator 73 that initiates the sequence of events can be set to 2, 20, 200 and 2,000 ms, with changes in the resistive network using an analog switch. Hence the on time for the LED's 41, 42 and 43 data acquisition IC and microprocessor 50 is only a small fraction of the oscillator cycle time, even with a 2 ms setting (500 Hz). The oscillator 73 also provides a timing sequence pulse to the microprocessor 50 and data acquisition IC's. The LED's require the highest power, ~200 mW for 40 mW optical power output. At the 2 ms per acquisition setting on the oscillator, the average power requirements for all three LED's is only 3 mW (1.5% duty cycle) and considerably less at a 2,000 ms setting. Similarly the duty cycle for the microprocessor and data acquisition IC in the power up setting has a duty cycle of only 2.5%. Hence the low power requirements of the infrared spectrometer means that it can be powered by four mercury C-cells (6 volts) which will allow an extended period of operation.

Various modifications may be made in details of design, and methodoly without departing from the scope and ambit of the invention.

CLAIMS

1. A non-invasive method for determining the absolute level of oxygen saturation in blood in deep tissue comprising the steps of:-

(i) irradiating a target area of tissue with radiation of at least two distinct wave lengths,

(ii) providing a first set of signals that represents the absorption of the radiation at each wave length,

(iii) perturbating the venous blood volume in the target tissue,

(iv) providing a second set of signals that represents the absorption of the radiation at each wave length after perturbation of the blood,

(v) subtracting the first set of signals from the second set of signals to provide a difference signal for each wavelength that represents the venous blood volume change as a consequence of the perturbation,

(vi) determining the ratio of the difference signals and comparing that ratio with the ratio determined in vitro to provide the absolute level of blood oxygen saturation.

2. A method according to claim 1 wherein the step of perturbating the venous blood in the target tissue is carried out at constant metabolism.

3. A method according to claim 2 wherein the perturbation step is voluntarily hydrostatically induced.

4. A method according to claim 2 wherein the perturbation step is affected by venous occlusion.

5. A method according to claim 1 wherein the step of perturbating the venous blood in the target tissue is carried out at changed metabolism.

6. A method according to claim 5 wherein the perturbation step is affected by electrically induced muscle contraction.

7. A method according to claim 5 wherein the perturbation step is affected by arterial occlusion.

8. A method according to claim 4 wherein the perturbation step is induced by voluntary muscle contraction.

9. A method according to claim 1 wherein the radiation is near infrared radiation.

10. A method according to claim 9 wherein the target tissue is irradiated with radiation at a first wavelength and at a second wavelength.

11. A method according to claim 10 wherein the first and second wavelengths straddle the isobestic wavelength of haemoglobin.

12. A method according to claim 10 wherein the target tissue is irradiated with radiation at a third wavelength which is shorter than the first and second wavelengths.

13. A method according to claim 12 wherein the third wavelength is used to distinguish between changes in arterial and venous volume.

14. A method according to claim 12 wherein the wavelengths are 760 ± 20nm; 800 ± 20nm and 840 ± 20nm.

15. A method according to claim 1 wherein the tissue is superficial muscle.

16. A method according to claim 1 wherein the tissue is the brain.

17. A method according to claim 1 wherein the tissue is muscle and including the step of estimating the muscle fibre type distribution from changes in the desaturation signal relaxation rates after the induction of isometric muscle contraction.

18. A method according to claim 1 wherein the tissue is muscle and including the step of tracking muscle energetics and vascular heamodynamics for electrically paced muscle during therapy training.

19. A method according to claim 1 wherein the tissue is muscle and including the step of tracking fatigue feedback signals for electrically powered muscle in paralysed limbs.

20. A method according to claim 1 wherein the tissue is the brain and the level of blood oxygen concentration is used to determine the level of hypoxia during apnea events.

21. Apparatus for determining the absolute level of oxygen saturation in blood in deep tissue comprising:-

a spectrometer adapted to direct to a target area of tissue radiation of at least two distinct wavelengths,

means for detecting the absorption of the radiation at each wavelength at a first state of the tissue,

means for providing a first set of signals that represent the absorption of the radiation at each wavelength at the first state of the tissue,

means for detecting the absorption of the radiation at each wavelength after voluntarily hydrostatically perturbating the venous blood volume in the target tissue,

means providing a second set of signals that represent the absorption of the radiation at each wavelength after perturbating of the blood,

means for subtracting the first set of signals from the second set of signals to provide a difference signal for each wavelength that represents the venous blood volume change as a consequence of the perturbation, and

means for determining the ratio of the difference signals and comparing that ratio with the ratio determined *in vitro* to provide the absolute level of blood oxygen concentration.

22. Apparatus according to claim 21 and including a pair of transmitting optodes and a receiving optode.

23. Apparatus according to claim 21 including three transmitting optodes and a receiving optode.

24. Apparatus according to claim 21 including a band having a first portion having a plurality of transmitting optodes and a receiving optode,

a second stretchable portion having an elongated strain gauge attached thereto adapted to provide a first electrical signal at its rest state and a second electrical signal when it is linlarly displaced upon stretching of the second portion of the band.

25. Apparatus according to claim 24 wherein the apparatus is adapted to power down when the stretchable portion resumes its rest state.

26. A band for use in determining the level of oxygen saturation in blood comprising:

a first portion having a plurality of transmitting optodes and a receiving optode,

a second stretchable portion having an elongated strain gauge attached thereto adapted to provide a first electrical signal at its rest state and a second electrical signal when it is linearly displaced upon stretching of the second portion of the band.

27. A band according to claim 26 wherein the transmitting optodes are positioned 30 ± 10 mn from the receiving optode.

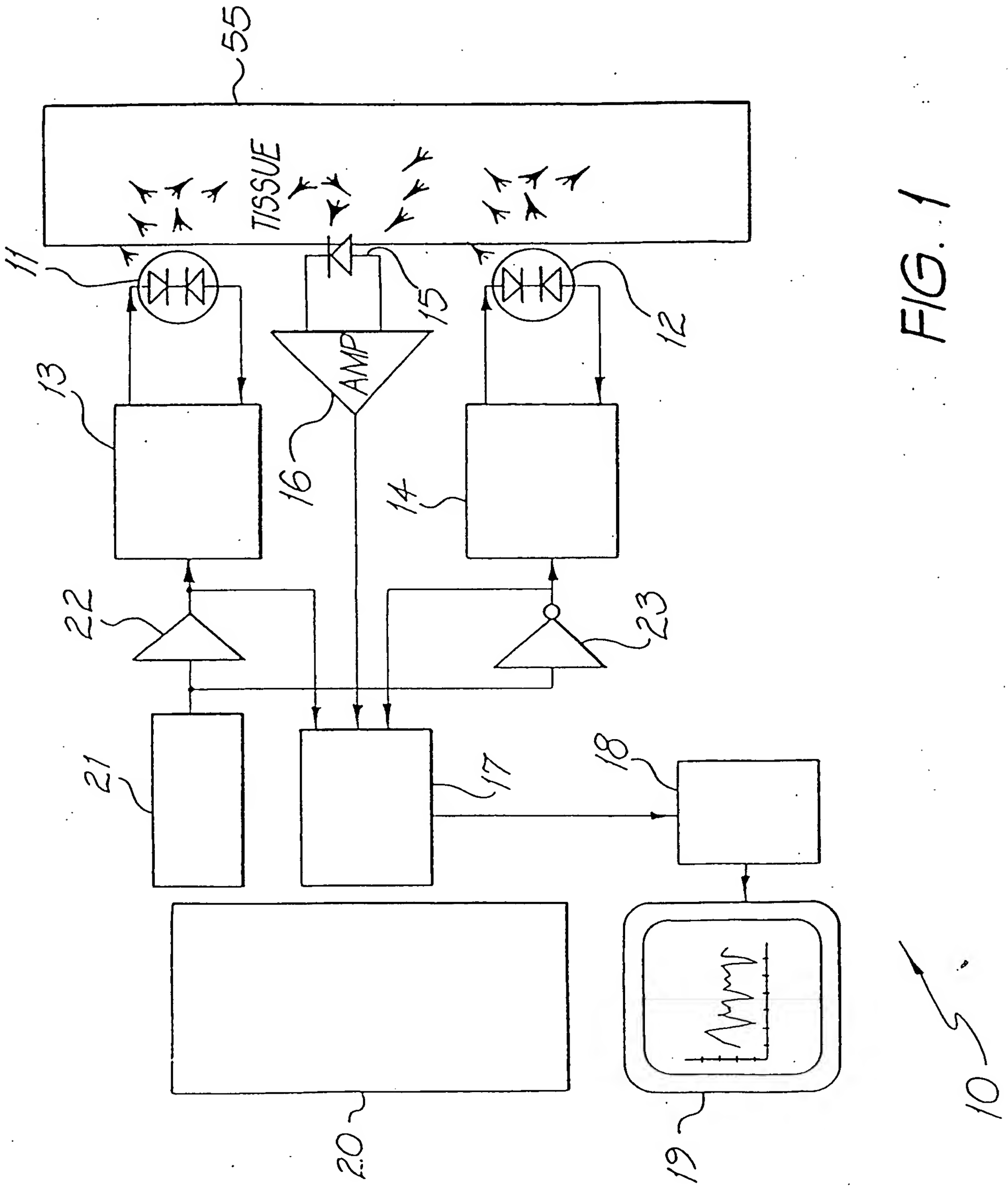
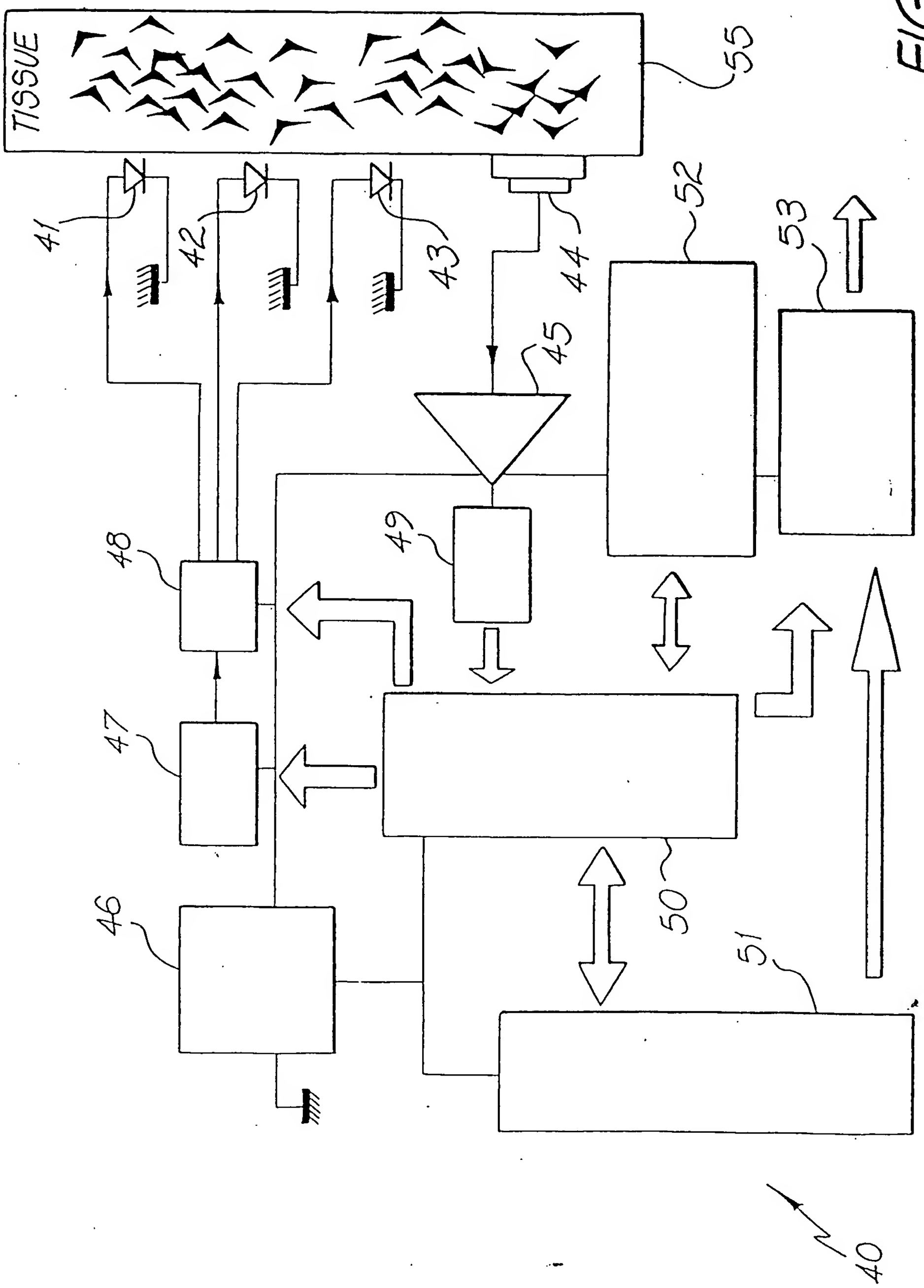


FIG. 1

FIG. 2



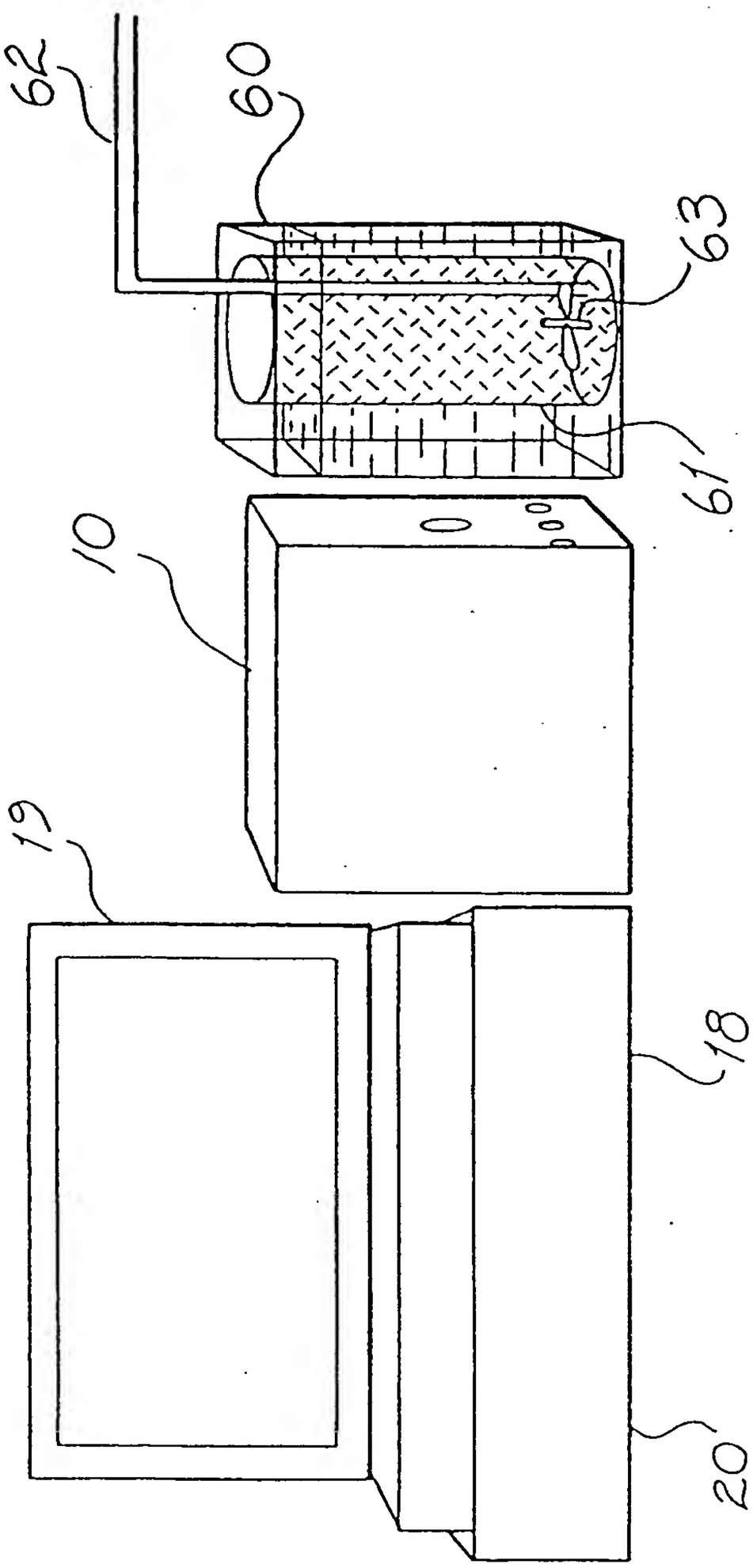


FIG. 3

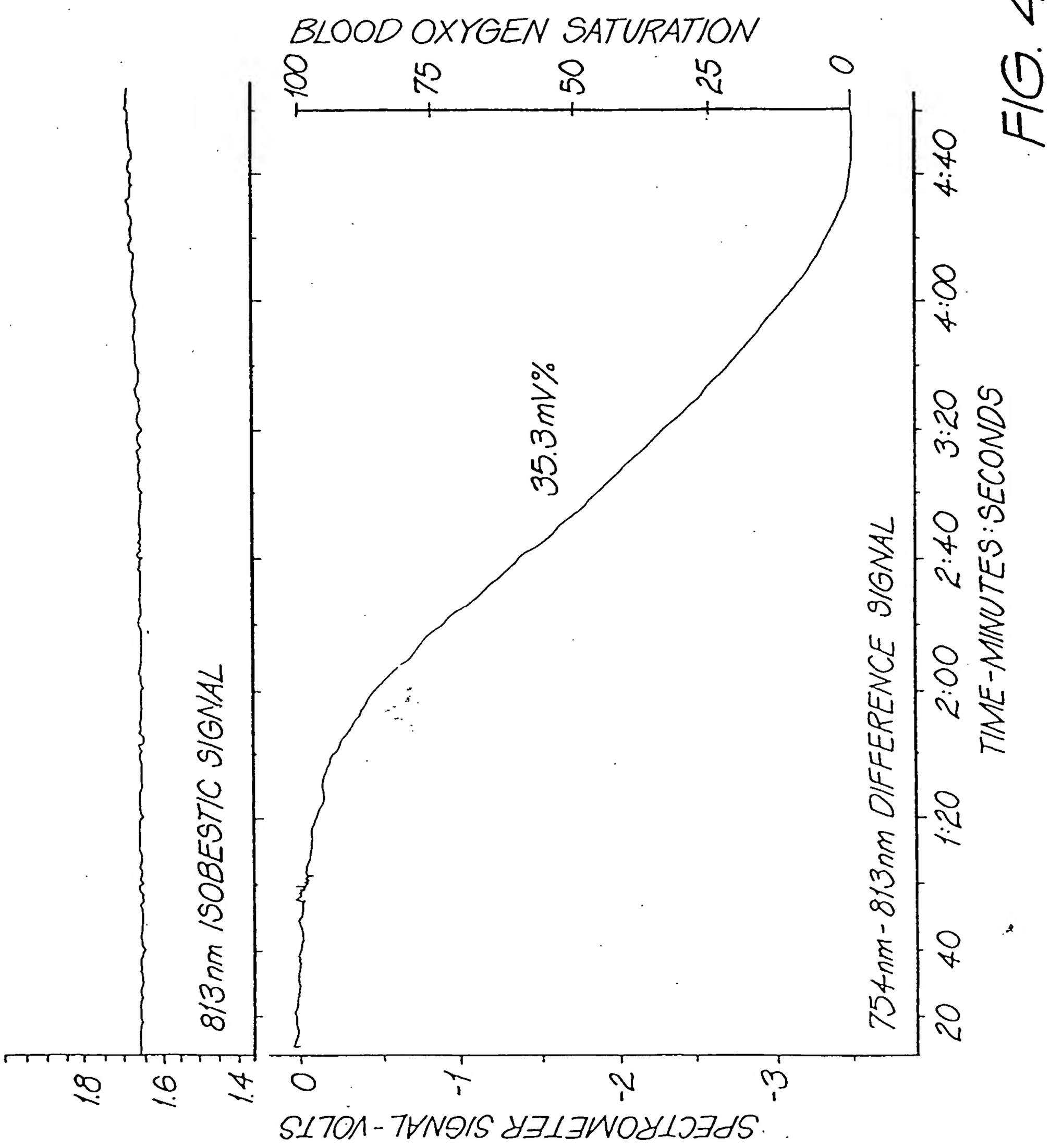

BLOOD OXYGEN SATURATION
100
75
50
25
0
35.3mV%
813nm ISOBESTIC SIGNAL
754nm-813nm DIFFERENCE SIGNAL
1.8
1.6
1.4
0
-1
-2
-3
SPECTROMETER SIGNAL-VOLTS
2:00
2:40
3:20
4:00
4:40
20
40
1:20
TIME-MINUTES:SECONDS

FIG. 4

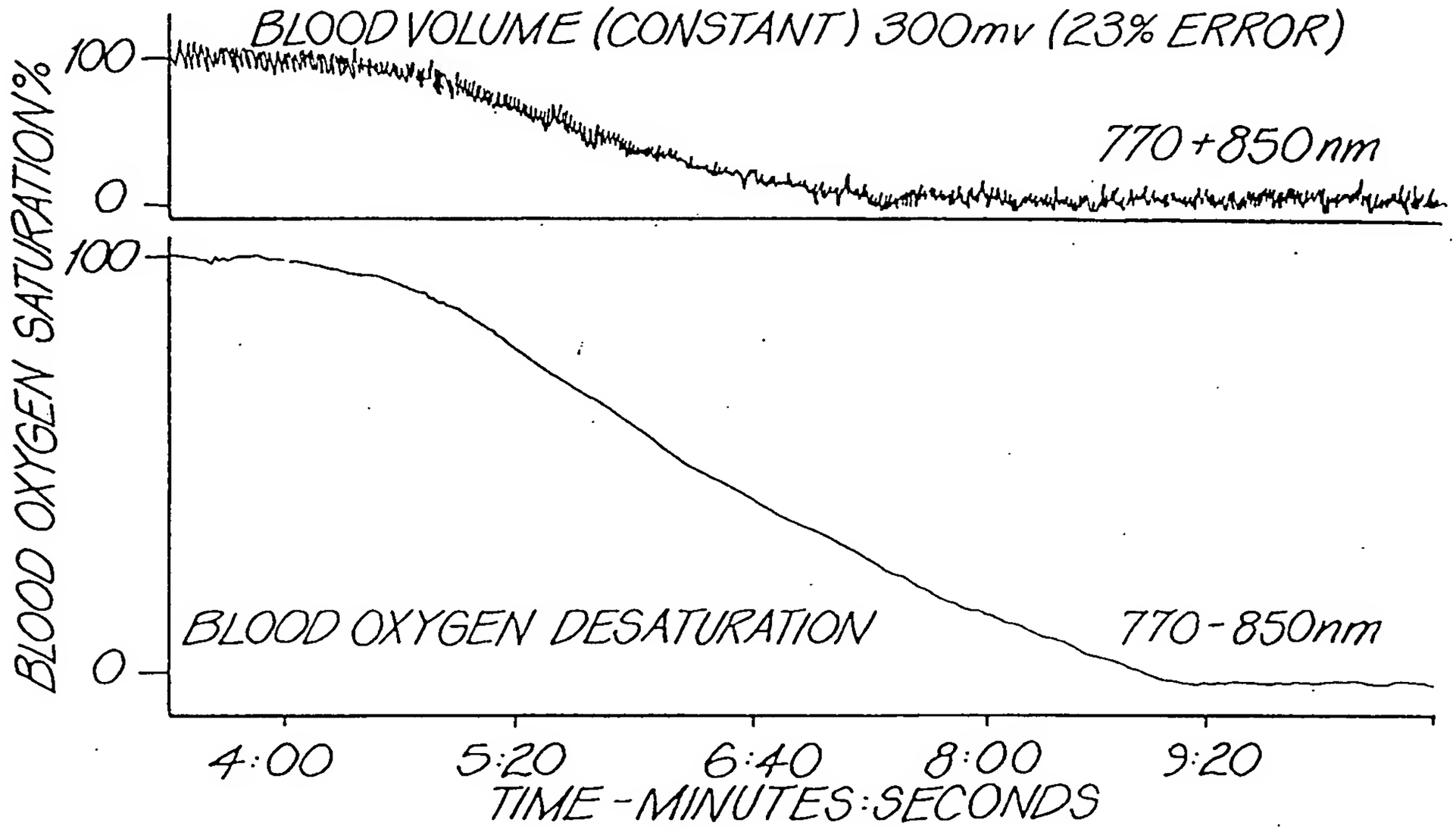

BLOOD VOLUME (CONSTANT) 300mv (23% ERROR)
100
0
770+850nm
100
BLOOD OXYGEN SATURATION%
0
BLOOD OXYGEN DESATURATION
770-850nm
4:00
5:20
6:40
8:00
9:20
TIME-MINUTES:SECONDS

FIG. 5A

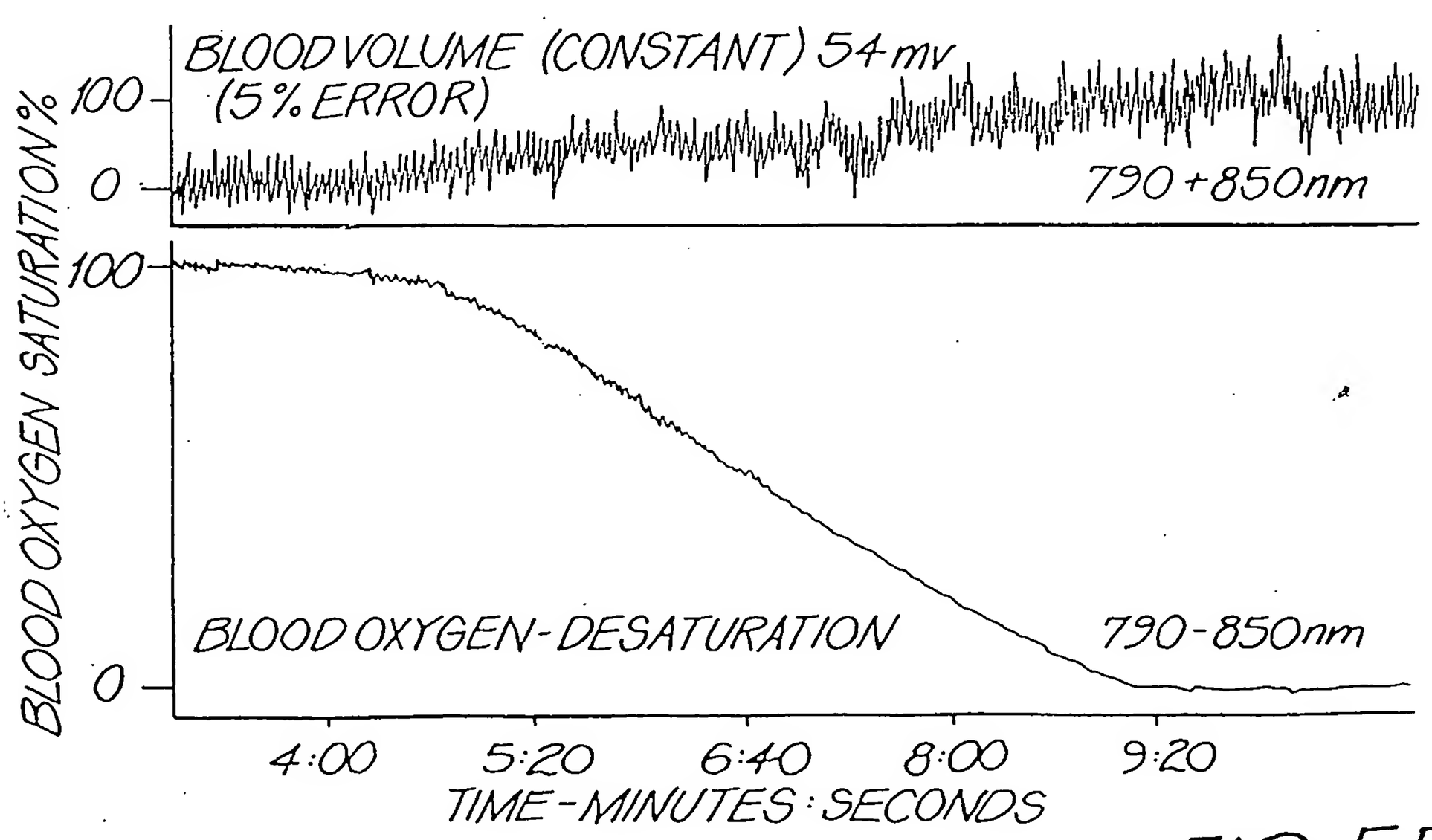

BLOOD VOLUME (CONSTANT) 54mv
(5% ERROR)
100
0
790+850nm
100
BLOOD OXYGEN SATURATION%
0
BLOOD OXYGEN-DESATURATION
790-850nm
4:00
5:20
6:40
8:00
9:20
TIME-MINUTES:SECONDS

FIG. 5B

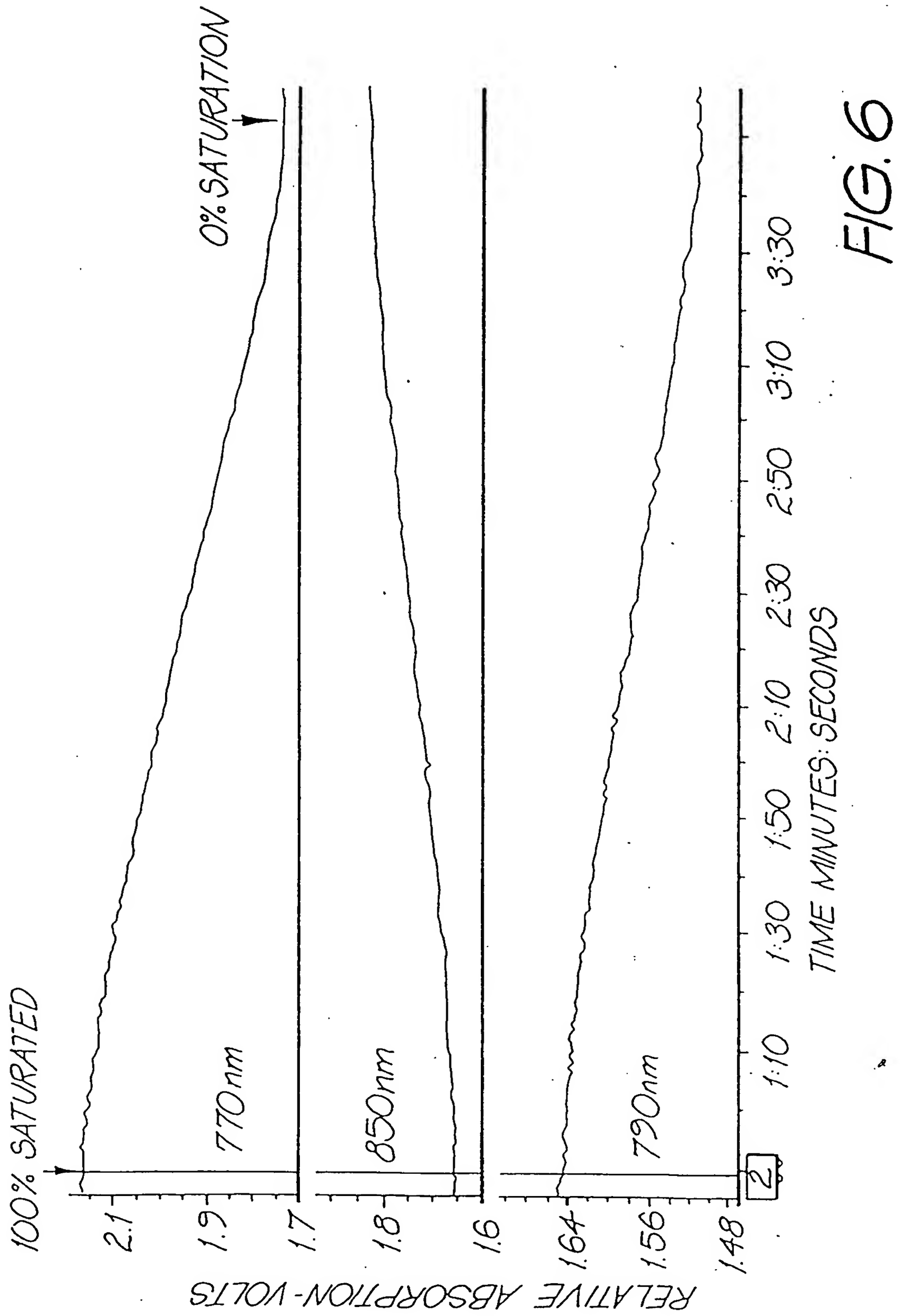

0% SATURATION
100% SATURATED
770nm
850nm
790nm
2.1
1.9
1.7
1.8
1.6
1.64
1.56
1.48
RELATIVE ABSORPTION-VOLTS
1:10
1:30
1:50
2:10
2:30
2:50
3:10
3:30
TIME MINUTES: SECONDS
2

FIG. 6

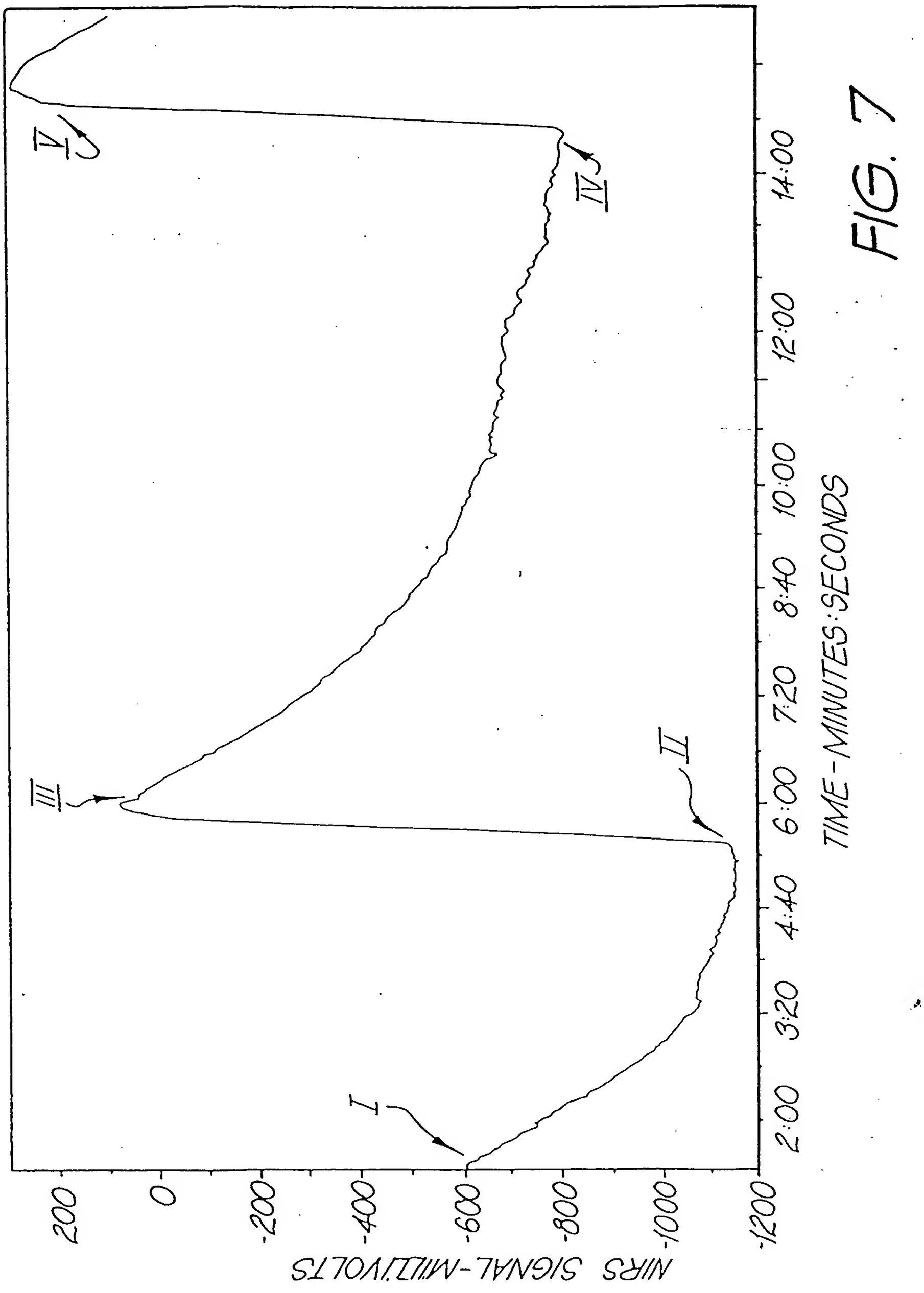

NIRS SIGNAL-MILLIVOLTS
200
0
-200
-400
-600
-800
-1000
-1200
TIME-MINUTES:SECONDS
2:00
3:20
4:40
6:00
7:20
8:40
10:00
12:00
14:00
I
II
III
IV

FIG. 7

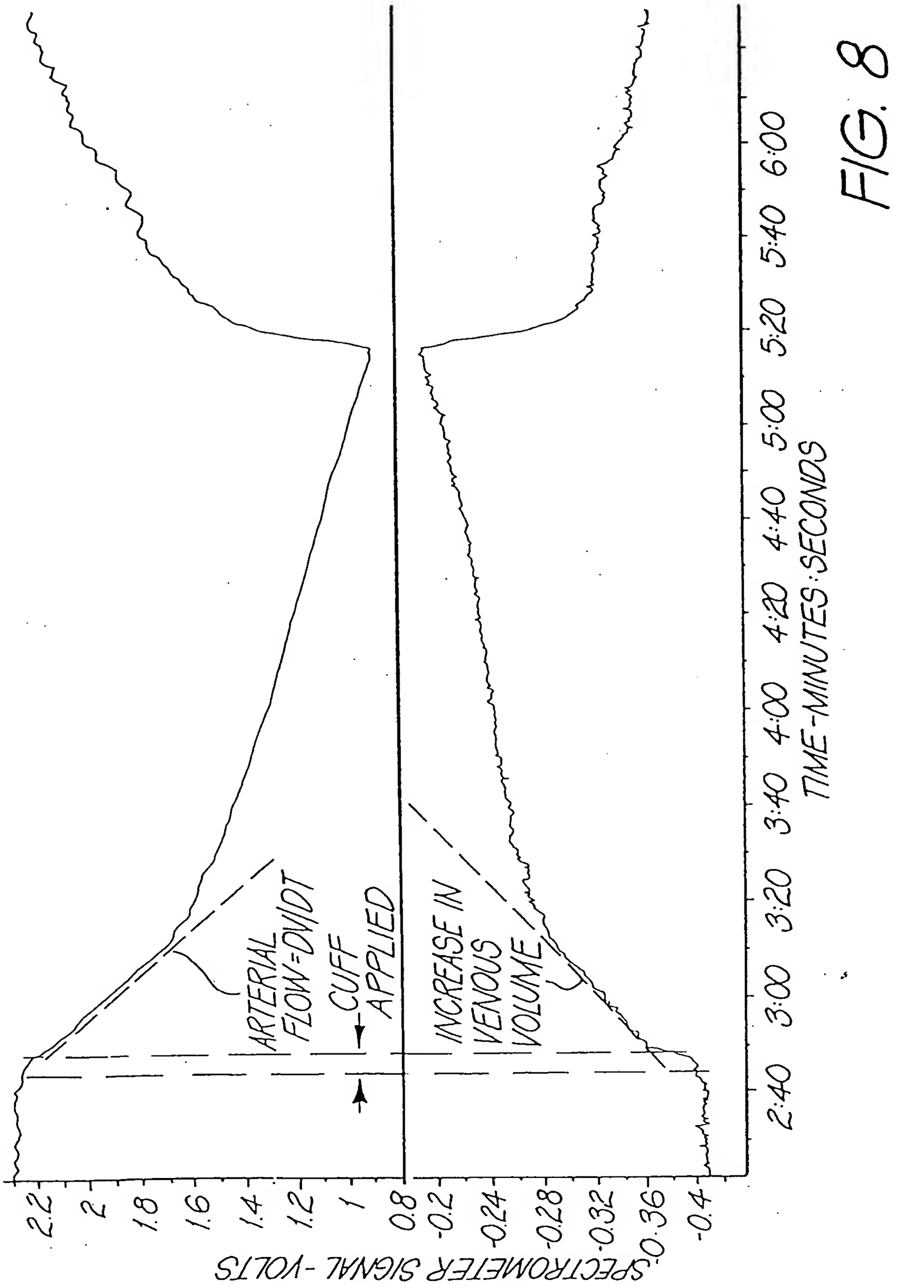

SPECTROMETER SIGNAL - VOLTS
2.2
2
1.8
1.6
1.4
1.2
1
0.8
-0.2
-0.24
-0.28
-0.32
-0.36
-0.4
TIME-MINUTES:SECONDS
2:40
3:00
3:20
3:40
4:00
4:20
4:40
5:00
5:20
5:40
6:00
ARTERIAL FLOW=DV/DT
CUFF APPLIED
INCREASE IN VENOUS VOLUME

FIG. 8

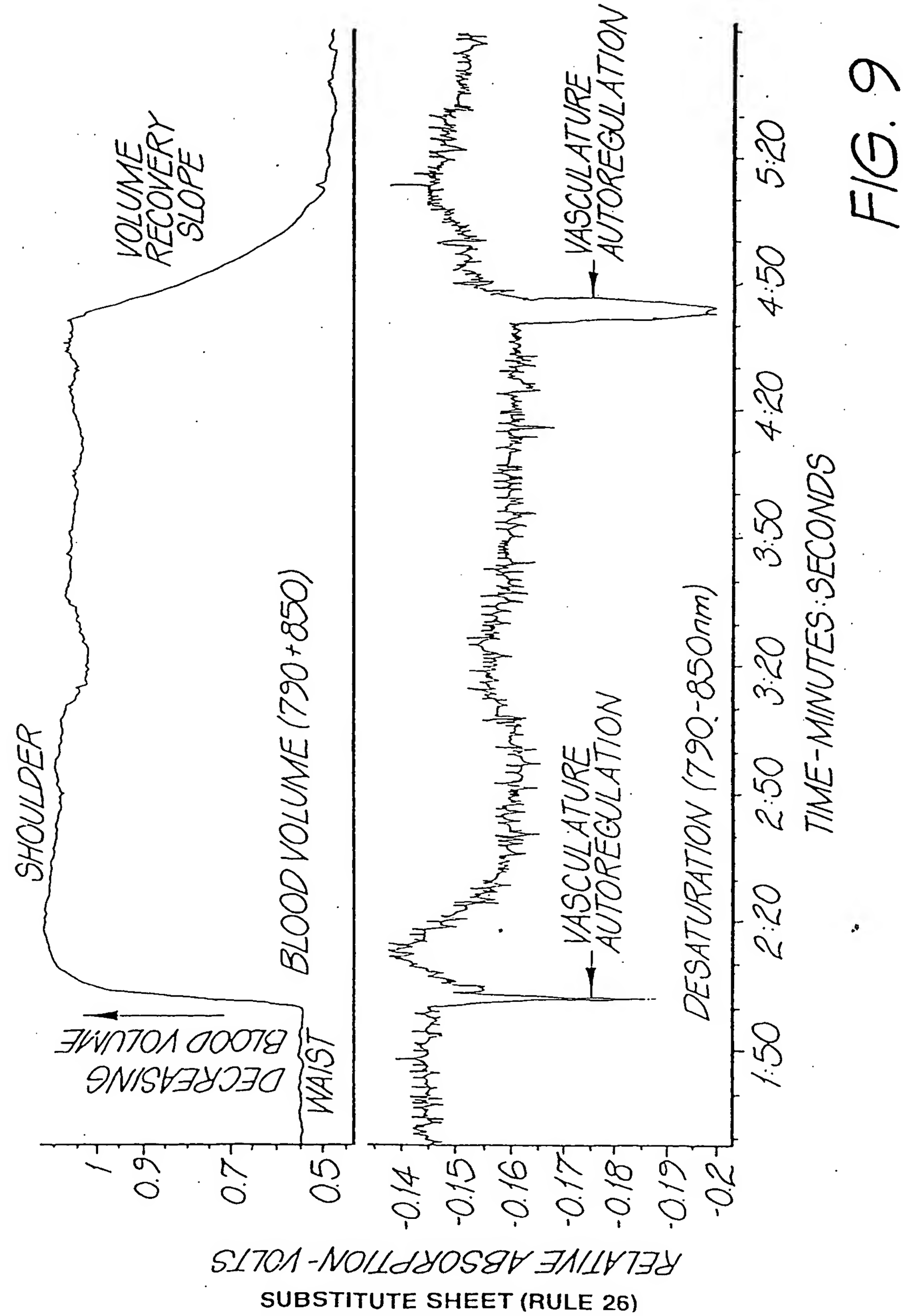

SHOULDER
DECREASING BLOOD VOLUME
WAIST
BLOOD VOLUME (790-850)
VOLUME RECOVERY SLOPE
1
0.9
0.7
0.5
RELATIVE ABSORPTION-VOLTS
-0.14
-0.15
-0.16
-0.17
-0.18
-0.19
-0.2
DESATURATION (790-850nm)
VASCULATURE AUTOREGULATION
VASCULATURE AUTOREGULATION
1:50
2:20
2:50
3:20
3:50
4:20
4:50
5:20
TIME-MINUTES:SECONDS

FIG. 9

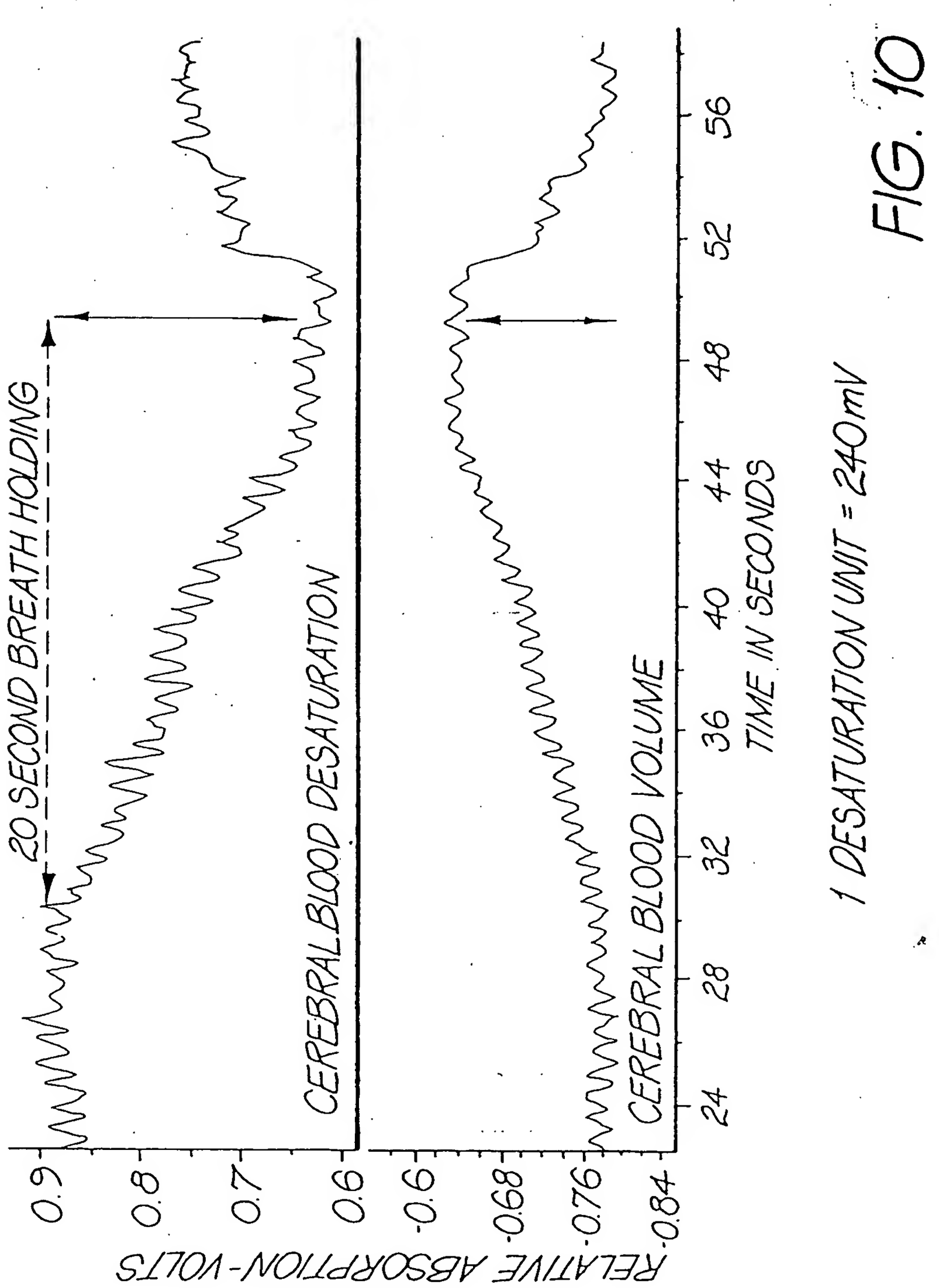

20 SECOND BREATH HOLDING
CEREBRAL BLOOD DESATURATION
CEREBRAL BLOOD VOLUME
RELATIVE ABSORPTION-VOLTS
0.9
0.8
0.7
0.6
-0.6
-0.68
-0.76
-0.84
24
28
32
36
40
44
48
52
56
TIME IN SECONDS
1 DESATURATION UNIT = 240mV

FIG. 10

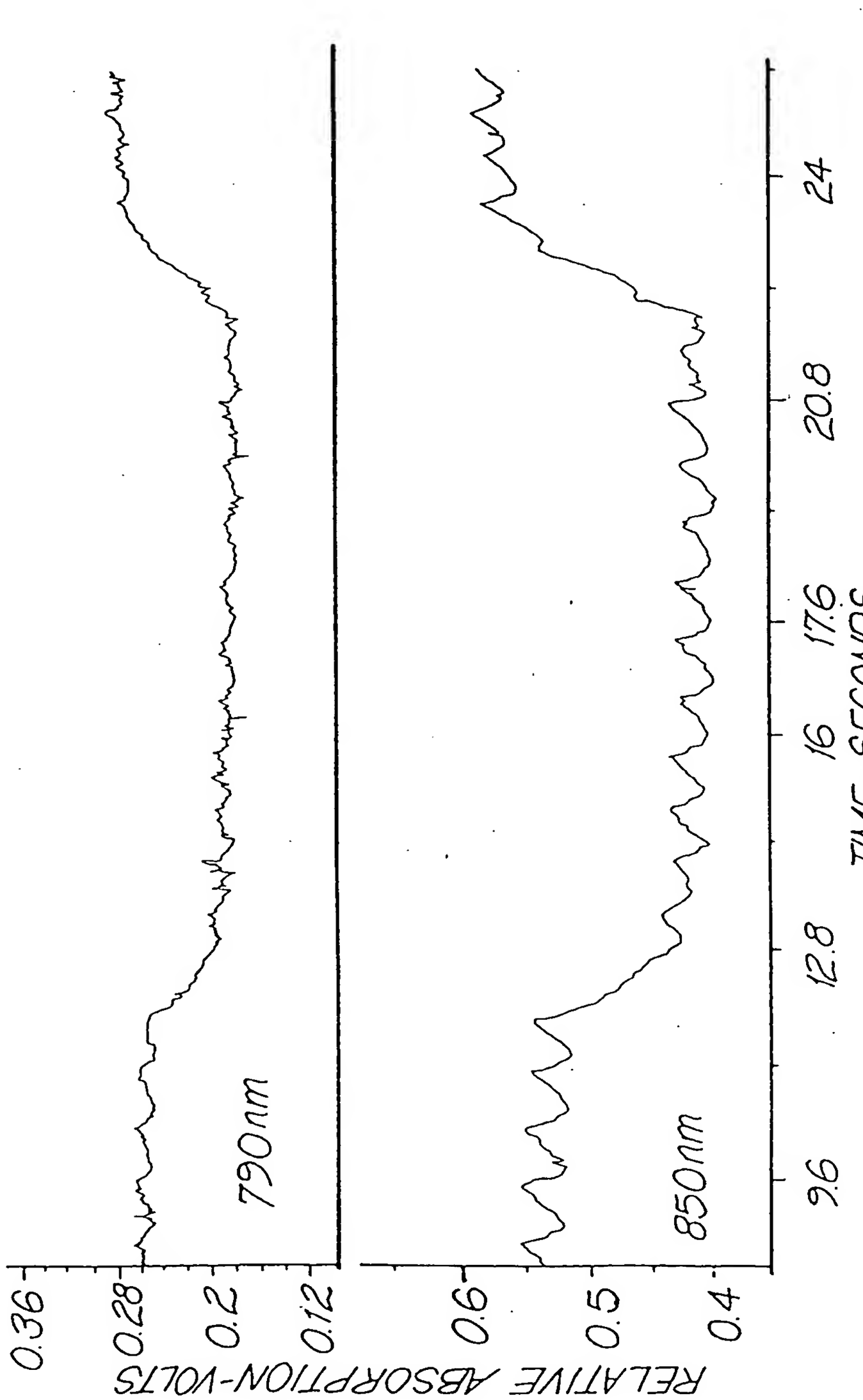

RELATIVE ABSORPTION-VOLTS
0.36
0.28
0.2
0.12
790nm
0.6
0.5
0.4
850nm
16
17.6
20.8
24
9.6
12.8
TIME-SECONDS

FIG. 10a

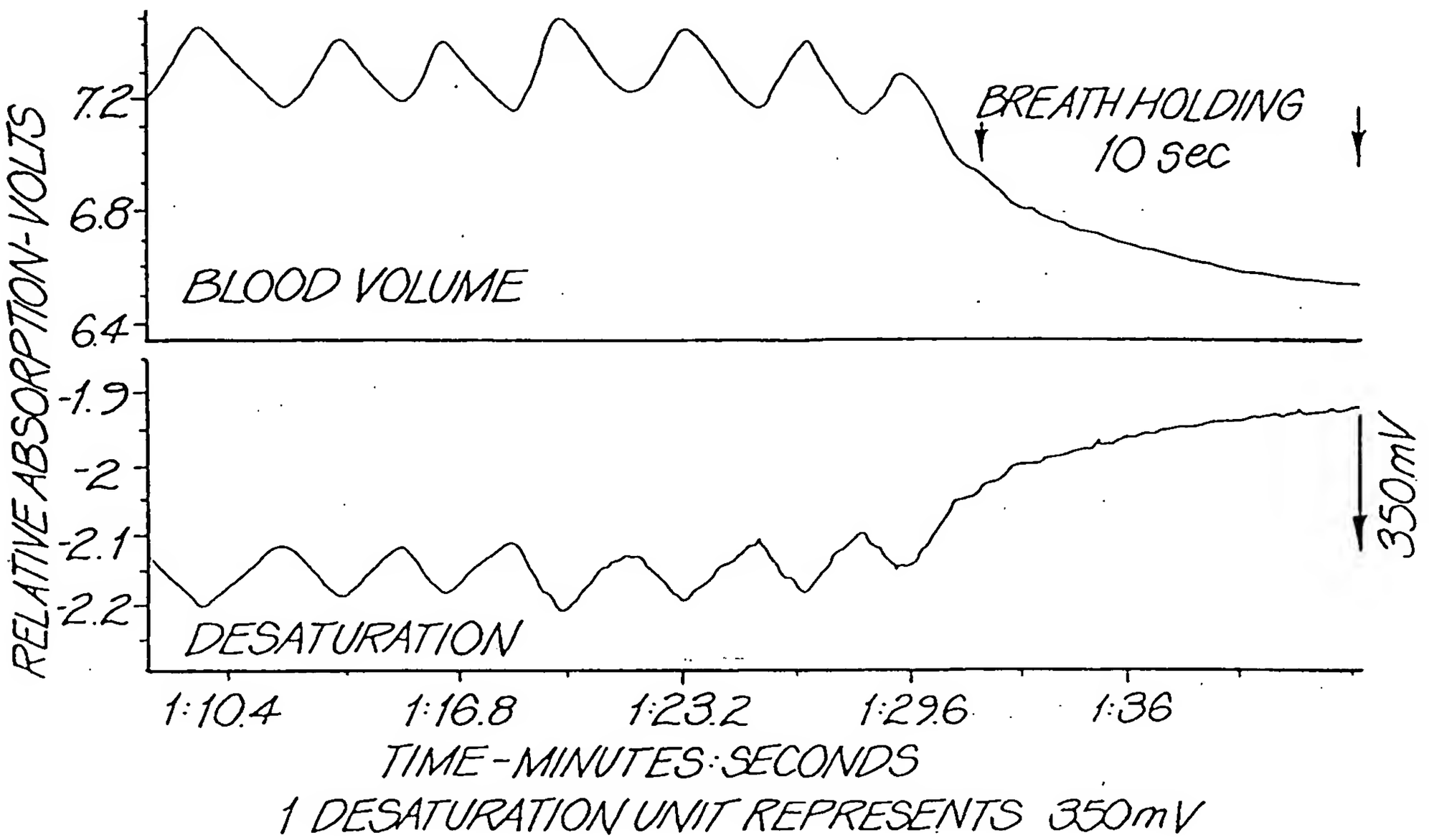


FIG. 11

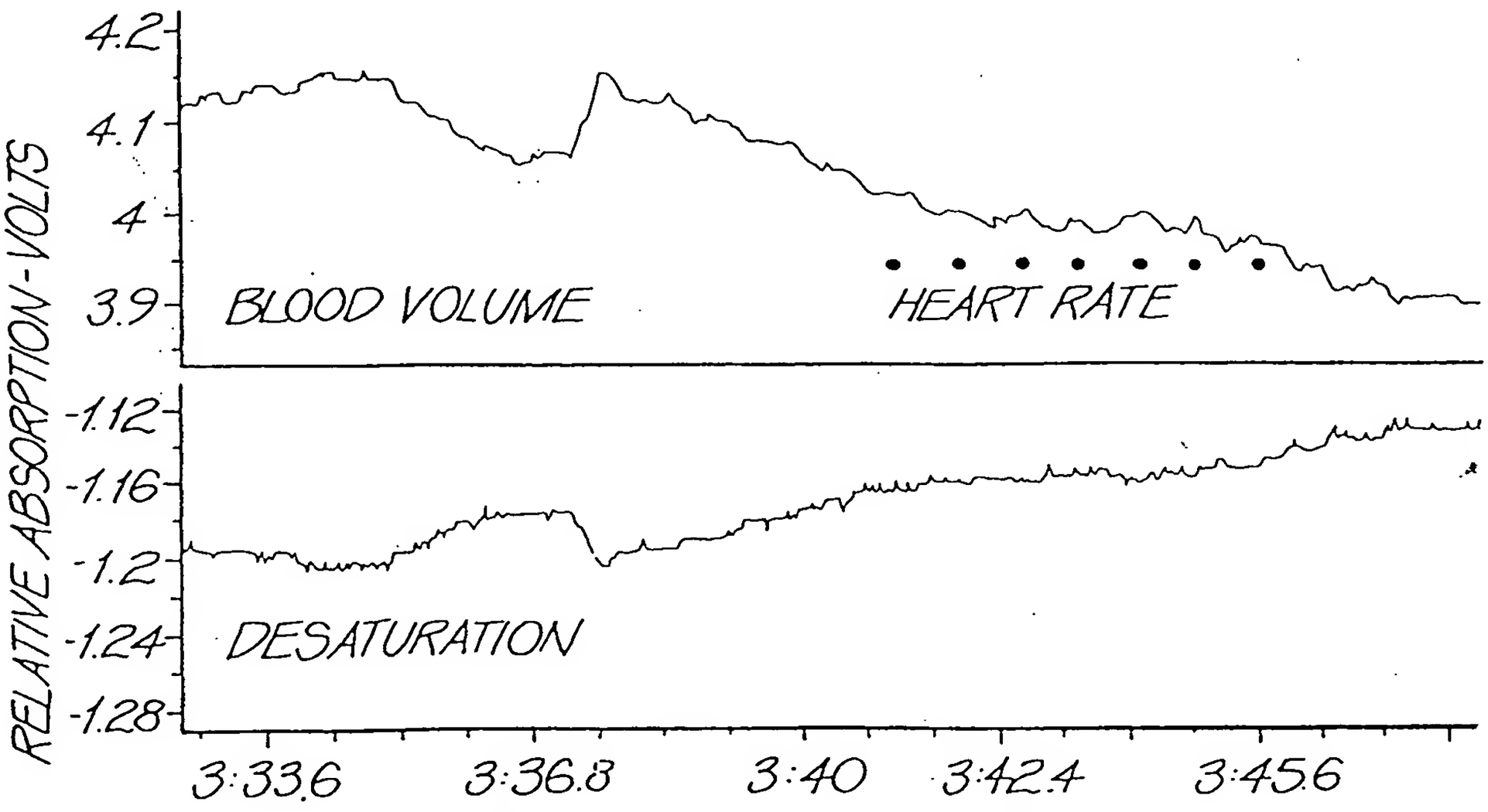


FIG. 11a

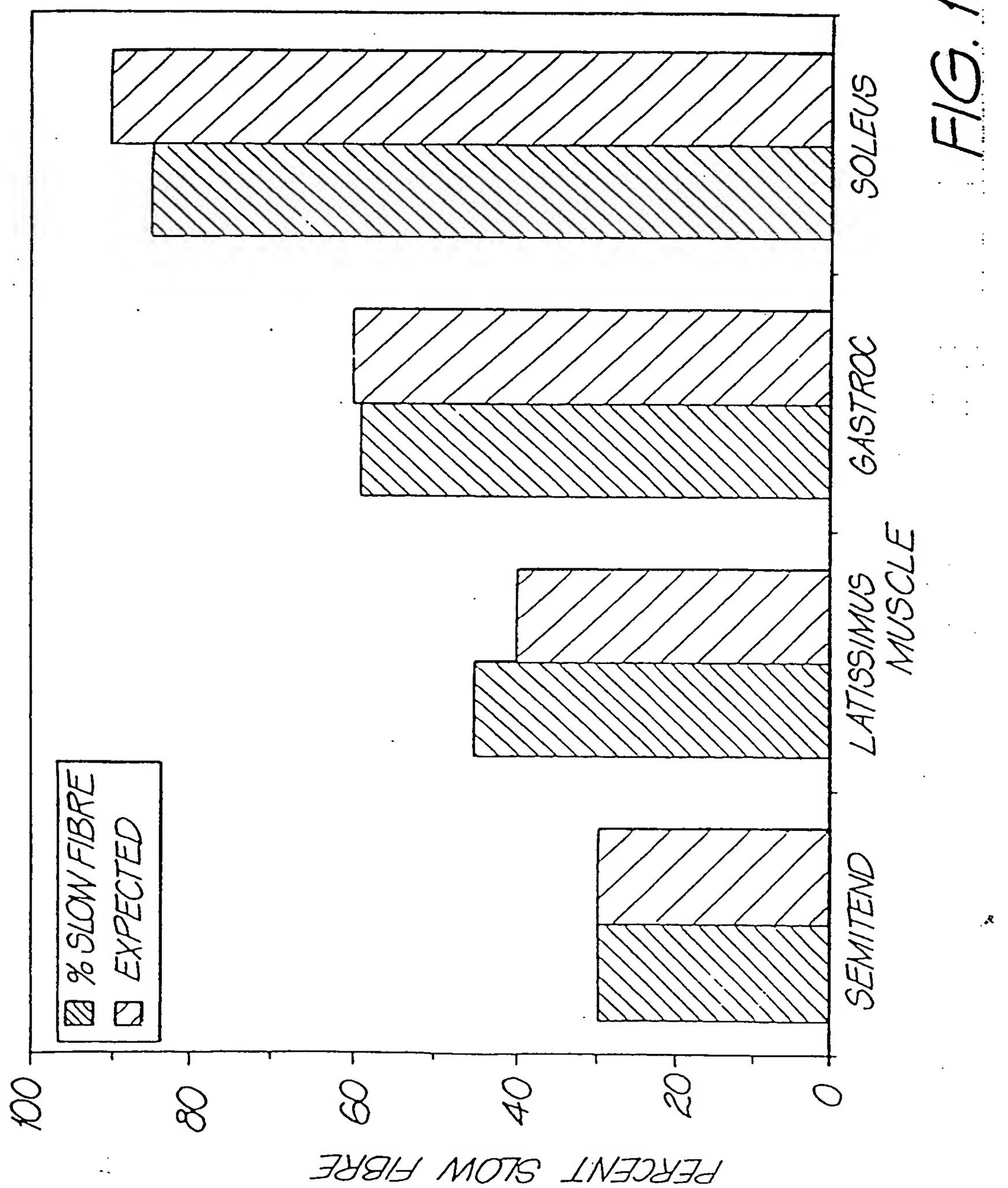

% SLOW FIBRE
EXPECTED
SOLEUS
GASTROC
LATISSIMUS MUSCLE
SEMITEND
100
80
60
40
20
0
PERCENT SLOW FIBRE

FIG. 12

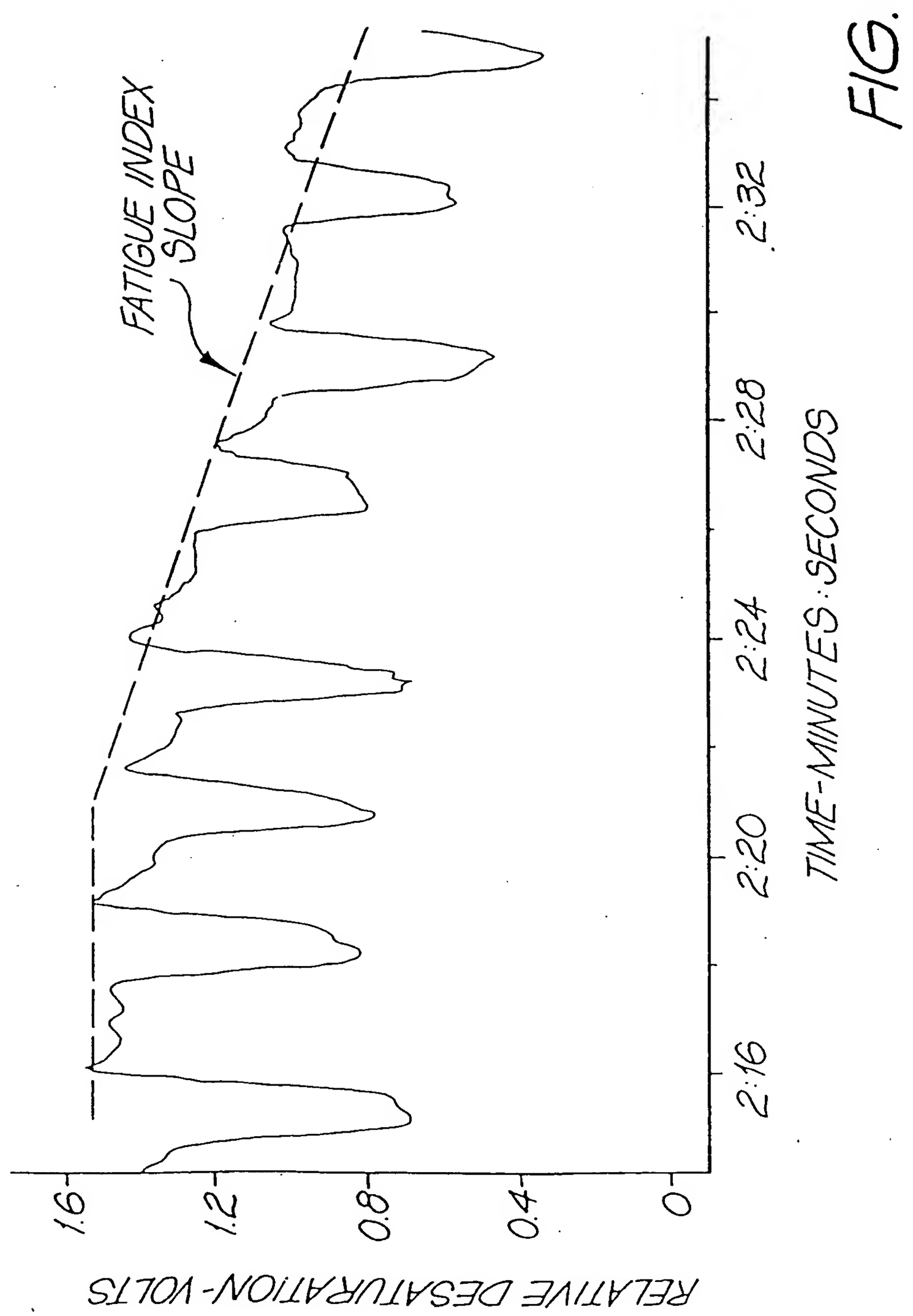

FATIGUE INDEX SLOPE
1.6
1.2
0.8
0.4
0
RELATIVE DESATURATION - VOLTS
2:16
2:20
2:24
2:28
2:32
TIME - MINUTES : SECONDS

FIG. 13

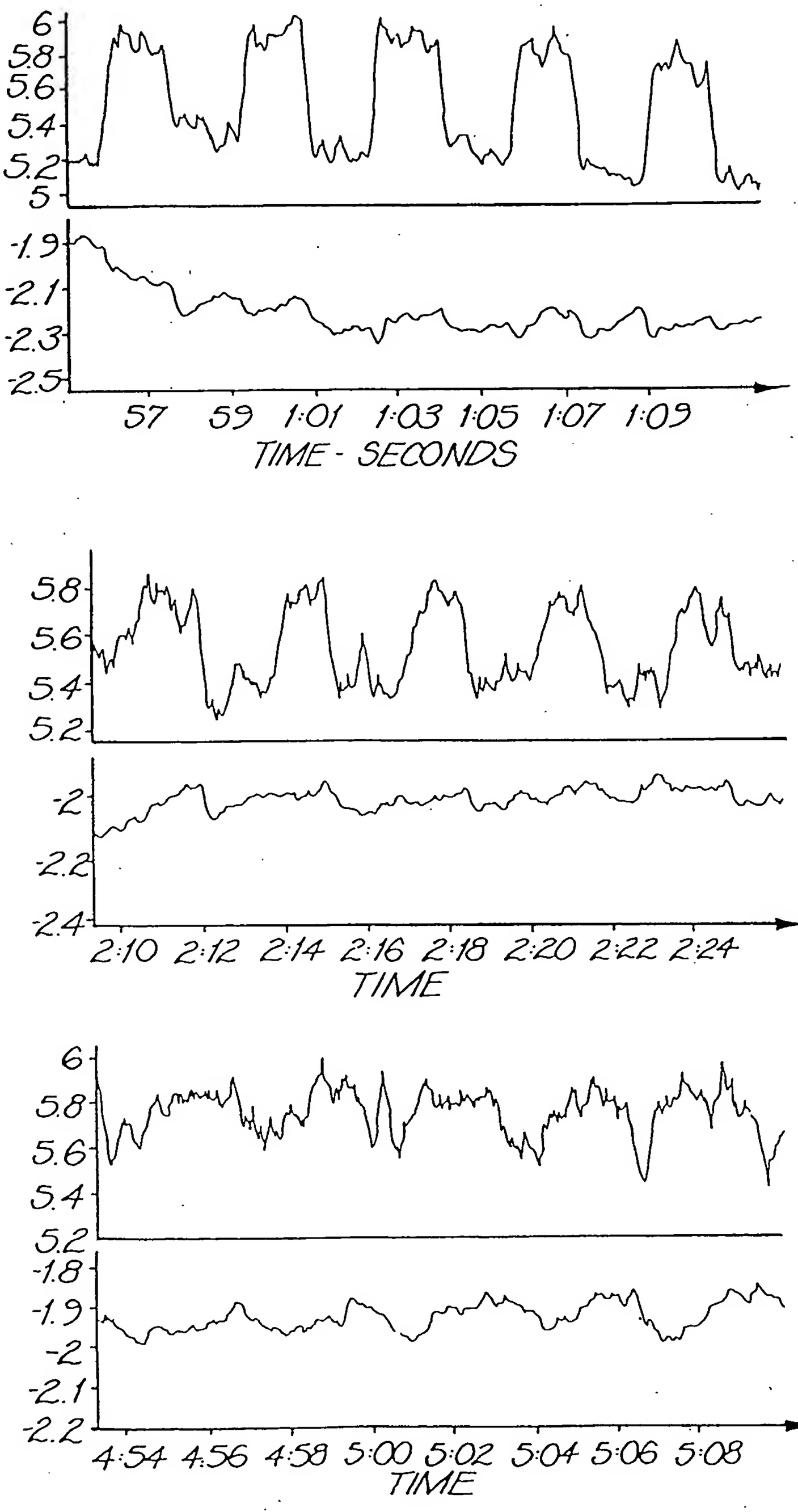

6
5.8
5.6
5.4
5.2
5
-1.9
-2.1
-2.3
-2.5
57 59 1:01 1:03 1:05 1:07 1:09
TIME - SECONDS
(A)
5.8
5.6
5.4
5.2
-2
-2.2
-2.4
2:10 2:12 2:14 2:16 2:18 2:20 2:22 2:24
TIME
(B)
6
5.8
5.6
5.4
5.2
-1.8
-1.9
-2
-2.1
-2.2
4:54 4:56 4:58 5:00 5:02 5:04 5:06 5:08
TIME
(C)

FIG. 14

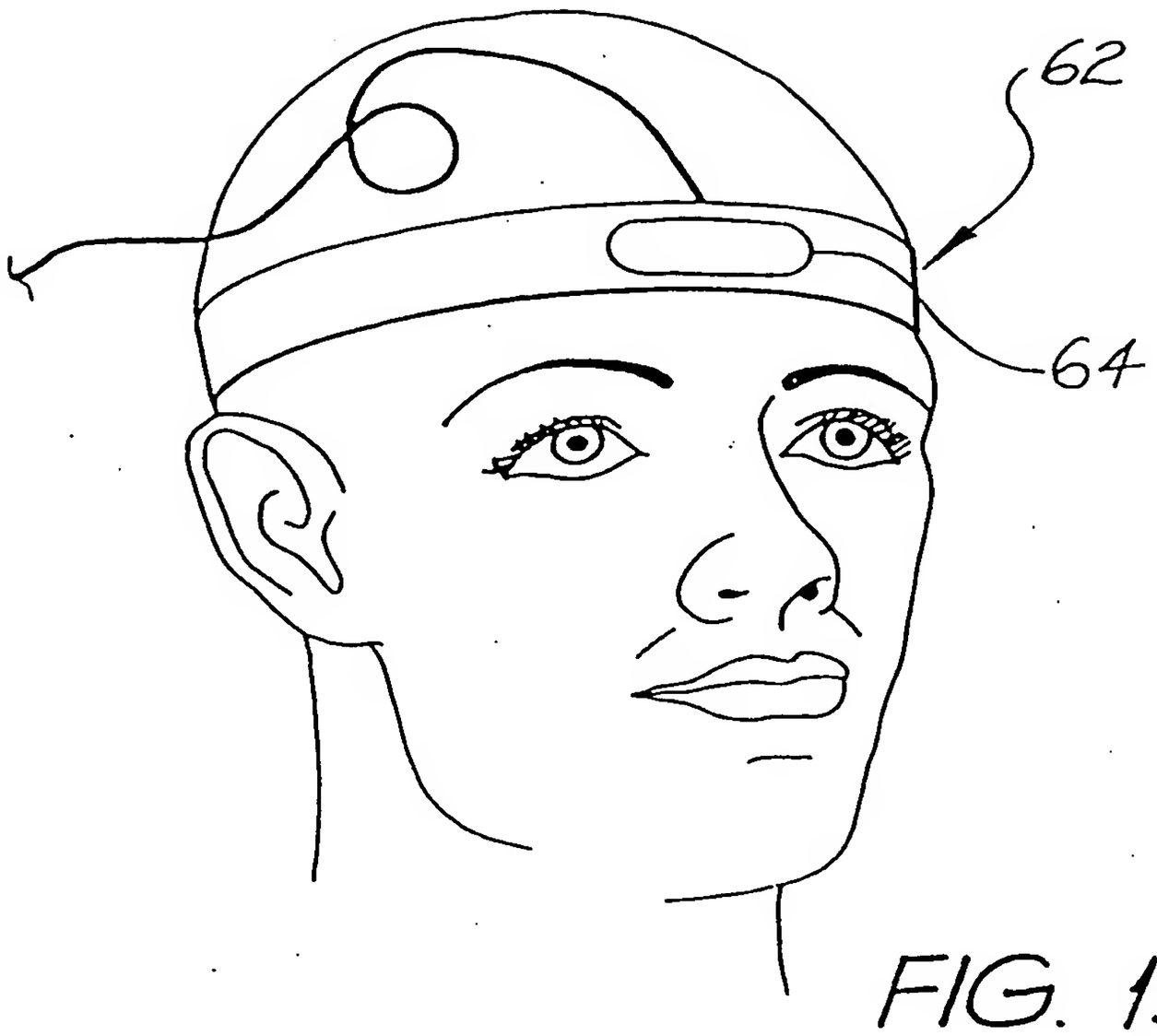


FIG. 15

FIG. 16

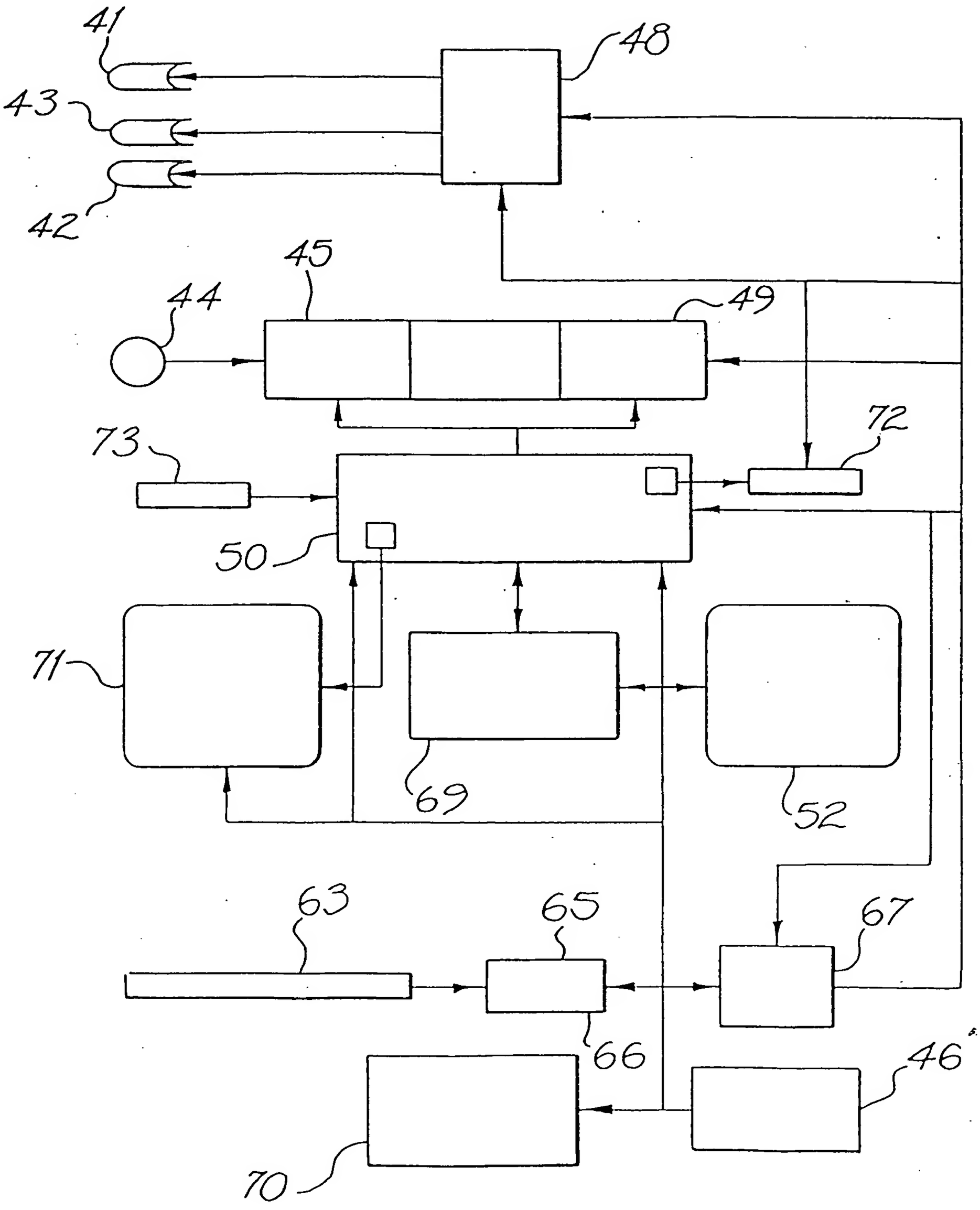


FIG. 17